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CONTENTS AND SUBJECT INDEX

Potassium in Familial Periodic Paralysis. Robert H. Pudenz, M.D.; J. F. McIntosh, M.D., and Donald McEachern, M.D., Montreal..2253

Mechanism of Action of Sulfanilamide. John S. Lockwood, M.D.; Alvin F. Coburn, M.D., and H. E. Stokinger, Ph.D., New York..2259

Pseudohypertrophic Muscular Dystrophy. Louis Scheman, M.D.; Philip Lewin, M.D., and Samuel Soskin, M.D., Chicago.....2265

Cardiac Irregularities. George Fahr, M.D., Minneapolis.....2268
Discussed by Drs. Kerr, Korns, Weisman, Dressler and Fahr.

Pathology of the Placenta. R. A. Bartholomew, M.D., Atlanta..2276
Discussed by Drs. Carlson, Hartman and Bartholomew.

The Use of Potassium Salts in Hay Fever. Benson Bloom, M.D., Tucson, Ariz.....2281

Toxic Hepatitis Due to Sulfanilamide. Curtis F. Garvin, M.D., Cleveland 2283

Radioactive Iron. P. F. Hahn, Ph.D.; W. F. Bale, Ph.D.; E. O. Lawrence, Ph.D., and G. H. Whipple, M.D., Rochester, N. Y...2285

Nicotinic Acid. W. H. Sebrell, M.D., and R. E. Butler, M.D., Washington, D. C.....2286

New York Syphilis Control. C. W. Clarke, M.D., and Theodore Rosenthal, M.D., New York.....2287

CLINICAL NOTES

Sensitization Reaction to Sulfanilamide. E. B. Rogers, M.D., El Paso, Texas.....2290

Red Blood Cell Increase in Pernicious Anemia. Raphael Isaacs, M.D.; F. H. Bethell, M.D.; M. C. Riddle, M.D., and Arnold Friedman, Ann Arbor, Mich.....2291

Quinine in Myotonia Congenita. R. B. Lonergan, M.D., and H. A. Paskind, M.D., Chicago.....2292

SPECIAL ARTICLE

Conferences on Therapy: I. Treatment of Pain.....2293

COUNCIL ON PHYSICAL THERAPY

Physical Characteristics of Short Wave Diathermy. Allan Hemingway, Ph.D., and K. W. Stenstrom, Ph.D., Minneapolis.....2298

COUNCIL ON FOODS 2303

EDITORIALS

Mode of Action of Sulfanilamide.2304

Formation of Milk Proteins....2305

CURRENT COMMENT

Salivary Influence on Galvanism.2306

Action of Prostatic Fluid.....2306

Sulfanilamide and Bacteriostasis.2306

BUREAU OF LEGAL MEDICINE AND LEGISLATION 2332

(Subject Index on next page)

ORGANIZATION SECTION

A. M. A. Study of Medical Care.2307

Graduate Education in Missouri.2308

Woman's Auxiliary.....2309

Medical Economic Abstracts...2310

A.M.A. SESSION — St. Louis — MAY 15-19, 1939

From LEADING SURGICAL CENTERS

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Complete Contents in SAUNDERS ADVERTISEMENT—Page 3

SUBJECT INDEX TO THIS ISSUE

The letters used to explain in which department the matter indexed appears are as follows: The Star (*) indicates an Original Article; "ab," abstract; "E," Editorial; "C," Correspondence; "Ml," Medicolegal; "ME," Medical Economics; "OS," Organization Section; "SS," Student Section.

A. M. A., hearings before grand jury..OS-2309
special broadcast on poliomyelitis.....OS-2309
Abortion, law on, Australia.....2319
Acid, nicotinic, orally, reaction to.....*2286
Actinomycosis, thymol therapy.....ab-2333
Adrenals, amyloidosis cause of Addison's disease.....ab-2335
cortex extract, familial paralysis attack after.....*2254; *2256
Alcoholism, quack treatment, Calif.....2312
American Association for Advancement of Science symposium on glycols.....2315
Anemia from sulfanilamide.....*2260
pernicious, treatment, standards for red blood cell increase.....*2291
radioactive iron and metabolism in.....*2285
Anesthesia, epidural block.....ab-2335
Aqueous Humor, blood chloride and.....ab-2339
Arrhythmia, extrasystoles, treatment.....*2273
Asthma, pollen, potassium salts in.....*2281
Atropine eye drops, idiosyncrasy to.....2327
paralysis (induced) in roentgen examination of digestive tract.....ab-2340
Attorneys, incomes.....OS-2311
Auricular Fibrillation, treatment.....*2268
Bacteriostasis and sulfanilamide.....E-2306
Beaumont's grave, pilgrimage to.....2313
Blood, ascorbic acid in, Lund-Lieck test..ab-2344
chloride in, and aqueous humor.....ab-2339
hypercholesteremia in placenta infarcts..*2276
potassium in familial periodic paralysis..*2253
Board Examinations.....2328
Boerhaave bicentenary; rare book exhibit...2312
Bonhoeffer, Karl, retired.....2318
Book Notices.....2329
Books Received.....Adv. page 30
Breast cancer, treatment.....2325
Brickner Lecture, Dr. Elsberg gave.....2313
British Heart Journal.....2316
Bureau of Investigation.....2322
Bureau of Legal Medicine and Legislation.2382
Cancer training center at Western Reserve.2314
Cellulitis of hand.....ab-2334
Christian, Henry A., to retire.....2313
Coccyx, variations in position.....ab-2337
Conferences on Therapy.....*2293
Correspondence.....2323
Council on Foods.....2303
Council on Physical Therapy.....2298
de Crinis, Max, appointment.....2318
Deaths.....2320
Diabetes Insipidus, posterior pituitary powder intranasally.....2327
Diabetes Mellitus, insulin in, lutein and lecithin effect on.....ab-2342
Diathermy, short wave, physical characteristics.....*2298
Digestive Tract, roentgenography, induced atropine paralysis in.....ab-2340
Digitalis in cardiac irregularities.....*2268
Diphtheria prevention in England.....OS-2310
Drugs, new, number in Germany.....2318
Dysentery, bacillary, in young infants..ab-2343
Dystrophy, muscular, pseudohypertrophic..*2265
Ear tuberculosis.....2317
Eclampsia, pathology of placenta.....*2276
Elsberg, C. A., gave Brickner Lecture.....2313
Embolism, pulmonary, slowly fatal.....ab-2340
Encephalitis, infectious, made reportable, Mass.....2313
Encephalomyelitis, equine, eastern.....ab-2336
Endocrine glands, testing functioning.....2324
Epilepsy and Little's disease.....ab-2341
surgical treatment.....ab-2337
Epinephrine, familial paralysis attack induced by.....*2253
Erysipelas, sensitivity to sulfanilamide....*2290
Erythrocytes, standards for increase.....*2291
Estrogens treatment of vulvovaginitis...ab-2342
Eyes inflammation.....ab-2333
Fire extinguishers, pyrene, dangers from..2326
Food allergy, potassium chloride in.....*2283
spoilage and menstruation.....2327
Foreign Letters.....2316
Fracture, ununited, relation to syphilis....2326
Frost, W. H., posthumous award of Sedgwick Medal.....2315
Gallbladder cancer, x-rays contraindicated..2326
inflammation (acute), immediate operation.....ab-2333
Gingivitis in children.....ab-2344
Glycols, symposium on.....2315
Gonorrhea urethritis, sulfanilamide for..ab-2344
Government Services.....2315
Hand, infections.....ab-2334
Hay Fever, treatment, potassium salts....*2281
Headache and vasodilators.....2327
Heart block, treatment.....*2274
rate irregularities, treatment.....*2268
Hospital construction by PWA.....OS-2311
Hypopharynx, tumors.....2317
Income levels and amount spent for medical service.....OS-2311
of physicians and others.....OS-2311
Infants feeding, ewe's milk.....2318
mortality in Germany.....OS-2311
Infections, pyogenic, low leukocyte count in.....ab-2335
rapidly spreading, effect of sulfanilamide.*2263
Intestines disease, Triboulet's reaction..ab-2343
iron absorption and excretion.....ab-2340
Iontophoresis.....2327
Iron, absorption and excretion.....ab-2340
radioactive, metabolism.....*2285
Jervey, James W., honored.....2314
Lactation, formation of milk proteins....E-2305
Larynx, polyps.....2317
tumors.....2317
Liver cancer, x-rays contraindicated for....2236
inflammation from sulfanilamide.....*2283
treatment, erythrocyte increase after...*2291
Lung edema, hypertonic dextrose solution in.....2326
Lymphosarcoma, treatment.....2327
McCormack, J. M., date of death.....2312
McIntire, Ross T., Surgeon General, U. S. N.....2315
Maggot therapy for osteomyelitis.....ab-2334
Marriages.....2319
Mastoid operations, facial paralysis with..ab-2335
Medical Education, graduate, in Missouri.....OS-2308
graduate lectures, New York.....2313
Medical Examinations and Licensure.....2328
Medical Service in, Sullivan County, Tenn.....OS-2307
income and amount spent for.....OS-2311
Medicine, socialized, and people, Australia.2319
Medicolegal Abstracts.....2332
Meetings, Coming Meetings.....2332
Meningitis, sulfanilamide for.....2317
Menstruation and food spoilage.....2327
disorders, endocrine etiology and treatment.....2324
Milk, ewe's, value in diet.....2318
proteins, formation.....E-2305
Myoglobin role in dystrophy.....*2265
Myotonia congenita, quinine in.....*2292
National Tuberculosis Association, plea for centralizing all activities under.....C-2323
New York syphilis control activities.....*2287
News.....2312
Nose, polyps, potassium therapy.....*2282
Ophthalmia, sympathetic, and panophthalmitis.....ab-2333
Optometry Practice Acts: licenses; revocation; advertising by employer.....Ml-2232
Orchestra, physicians', Brooklyn.....2313
Organization Section.....2307
Osteomyelitis, hematogenous, maggot therapy for.....ab-2334
Otorhinolaryngology, French Congress.....2317
Ovary, testing functioning.....2324
Pain, relief of, Conferences on Therapy..*2293
Pancreatic Extract in ureter calculi.....2324
in muscular dystrophy.....*2266
Paralysis, facial, complicating mastoid operations.....ab-2335
familial periodic, potassium in.....*2253
spastic, and epilepsy.....ab-2341
Paronychia.....ab-2334
Pellagra, nicotinic acid orally in, reaction to.....*2286
Peptic Ulcer, granulomatous and tuberculous.....ab-2339
Phosgene, dangers from fire extinguishers..2326
Physicians, incomes.....OS-2311
positions open, Calif.....2312
Placenta, pathology.....*2276
permeability to sulfanilamide.....ab-2336
Pleura tumors, endothelioma of pleura..ab-2339
Pneumonia in pregnancy, serum cures..ab-2336
Poliomyelitis, extent in Germany.....2317
National Foundation extends organization.2315
special radio broadcast on.....OS-2309
Potassium metabolism in familial periodic paralysis.....*2253
salts, use in hay fever.....*2281
Pregnancy, pneumonia in, serum cures..ab-2336
polyneuritis and vitamin B_1.....ab-2343
respiration and blood oxygen during..ab-2342
toxemia, placenta pathology.....*2276
toxemia, progesterone for.....ab-2338
Prizes, Fiske Fund Essay.....2314
Sedgwick Medal, posthumous award.....2315
Prostate fluid, germicidal action.....E-2306
Psychoanalysis, lectures on, Chicago.....2312
Purpura haemorrhagica from sedormid.....2316
Pyrene fire extinguishers, dangers from...2326
Queries and Minor Notes.....2324
Quinidine for cardiac irregularities.....*2268
Quinine treatment in myotonia congenita.*2292
Radio Broadcasts.....2309
Radioactive iron.....*2285
Rectum, ulcer due to uterus cancer.....2316
Respiration during pregnancy.....ab-2342
Saliva effect on galvanism.....E-2306
Scarlet Fever, quarantine reduced, N. J....2313
Sedormid, toxic effects.....2316
Society Proceedings.....2332
Southwestern Medical Association.....2315
Spine, anomalies.....ab-2341
osteomalacia, vitamin D and calcium for.....ab-2344
State Board Examinations.....2328
Sterilization, Sexual, cauterizing uterine cornu.....ab-2338
Stomatitis, recurrent, caused by yeast.....2325
Streptococcus, hemolytic, reappearance after sulfanilamide.....*2261; *2262
infections, serum therapy.....ab-2334
Sulfanilamide, action of,.....*2259; E-2304
bacteriostasis and.....E-2306
mono-ethanol, absorption; excretion...ab-2335
passage, through human placenta.....ab-2336
sensitization reaction to.....*2290
toxic hepatitis due to.....*2283
toxicity.....*2259
treatment of gonorrhea with 1162 F. 40 R. P., and sulfanilamido-pyridine.ab-2341
treatment of meningitis.....2317
treatment of urethritis.....ab-2344
Sulfanilyl-sulfanilamide, absorption and excretion.....ab-2335
Surgery, operating room, air-borne bacteria in.....ab-2338
Syphilis, control activities, New York City.*2287
relation to ununited fracture.....2326
Tachycardia, paroxysmal, treatment.....*2273
Teeth fillings, salivary influence on galvanism.....E-2306
Temporal Bone, changes in Ménière's syndrome.....ab-2339
Tennessee, study of medical care.....OS-2307
Testis, function test.....2324
Therapy, Conferences on.....*2293
Thyroidectomy, preoperative vitamin B_1..ab-2337
Tonics and Sedatives.....Adv. page 24
Torticollis.....2325
Triboulet's Reaction evaluated.....ab-2343
Tuberculosis allergy without infection..ab-2336
mortality rate low; Christmas Seal.....2315
pulmonary, artificial pneumothorax in, sedimentation and serologic reactions.ab-2340
useless duplication.....C-2323
Tularemia outbreaks, U. S.....2315
Tumors, tar, effect of dextrose on.....ab-2344
Ureter calculi, pancreatic extract in.....2324
Urethritis, sulfanilamide for.....ab-2344
Urinary Tract, calculi, phosphate.....ab-2343
infections, calcium mandelate for.....ab-2344
Urine creatine in muscular dystrophy....*2266
Uterus cancer (cervical incipient), latent period.....ab-2342
cancer, rectal ulcer due to.....2316
cauterizing cornu.....ab-2338
Van Etten, Nathan B., honored.....2313
Vasomotor Mechanism, vasodilators and headache.....2327
Vertigo, Ménière's syndrome, pathology.ab-2339
obscure attacks.....2325
Vital Statistics, morbidity, England.....2316
Vitamin B_1 and pregnancy polyneuritis.ab-2343
B_1 preoperative and thyroidectomy....ab-2337
C in healthy children; in those with gingivitis.....ab-2344
D treatment of spinal osteomalacia...ab-2344
Volhard, Franz, retired.....2318
Vulvovaginitis in little girls, Progynon B for.....ab-2342
Western Reserve, cancer training center...2314
Woman's Auxiliary.....2308
Women, health of, factors undermining..ab-2340
Workmen's Compensation Acts: mental sequelae retarding recovery from injury.....Ml-2232
Wounds, infected, topical agents for....ab-2333

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THE ROLE OF POTASSIUM IN FAMILIAL PERIODIC PARALYSIS

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JOHN F. McINTOSH, M.D.
AND
DONALD McEACHERN, M.D.
MONTREAL

This rare but fascinating disease was first described by Cavaré [1] in 1853 and later in 1874 by Hartwig,[2] who named it intermittent spinal paralysis. It is characterized by recurrent attacks of flaccid paralysis affecting mainly the muscles of the trunk and limbs, during which the deep reflexes disappear and the muscles become inexcitable to electrical stimulation. Attacks usually come on during sleep without previous warning; they last from a few hours to three or four days. In the interval muscular power is normal and the patient is entirely well. Attacks first make their appearance during childhood or adolescence and become less frequent or disappear in later life. Males are twice as often affected as females. Sporadic cases have been reported, but the condition is usually hereditary; Holtzapple [3] has described seventeen cases in four generations of the same sibship. Many theories have been advanced to explain these weird and crippling seizures.

The most comprehensive study of the disease has been made by Shinosaki,[4] who published his observations in twenty-four cases. Among the more important observations were the frequent (62 per cent) association of the disease with thyroid struma and the tendency for attacks to occur after administration of thyroid, epinephrine or diets high in carbohydrate. Hyperglycemia was often observed during the early stages of spontaneous attacks, and albuminuria was present during attacks in 73 per cent of the cases. Shinosaki carried out many ingenious experiments and concluded that the disease was a polyglandular syndrome in which the thyroid played an important part.

Our interest in the condition, and especially in the role of potassium, was aroused by the work of Herrington.[5] He reported the cases of two brothers who averted paralysis by the ingestion of potassium citrate when prodromal symptoms appeared but he offered no explanation of the mechanism and carried out no metabolic studies. In 1901 Singer and Goodbody [6] administered potassium acetate to a patient with this disease in an attempt to promote diuresis and noted that attacks of paralysis became less frequent and severe. Holtzapple [3] had similar success with potassium bromide but attributed it to a sedative action of the bromide. Moreover, Biemond and Daniels [7] found a serum potassium value of 13.38 mg. per hundred cubic centimeters in a mild spontaneous attack and a value of 17.87 mg. during an interval but did not appreciate the significance of their results.

Since the commencement of our work, Aitken, Allott, Castleden and Walker [8] have reported their careful study of a patient with this disease. More recently Ferrebee, Atchley and Loeb,[9] Allott and McArdle [10] and Gammon [11] have published their observations. In agreement with their results we have found that attacks are associated with a marked fall of serum potassium and that administration of adequate amounts of potassium salts brings about rapid recovery.

We have produced attacks by administration of dextrose, epinephrine and ephedrine and have brought about recovery by injection of choline chloride carbamate (doryl) and acetyl-β-methylcholine chloride (mecholyl). Studies of electrolyte balance and the results of intravenous and intra-arterial injections of potassium chloride have thrown light on the mechanism of the attacks. A defect of creatine metabolism has also been observed, as noted in our preliminary report.[12]

L. H., a youth aged 18, has had recurrent attacks of paralysis involving the muscles of the trunk and extremities, and to a lesser extent the muscles of mastication and expression, since the age of 1[illegible]. Similar attacks have occurred in the father, one brother and one sister.

The attacks almost invariably begin during sleep and last from twenty-four to forty-eight hours. He knows of no precipitating factors. Between the attacks he is active and feels perfectly well. Examination during the interval elicits no abnormality. Of late, attacks have been occurring several times each month.

The weakness begins in the muscle groups of the back and hips and within one or two hours extends to involve the neck,

From the Montreal Neurological Institute and the University Clinic, Royal Victoria Hospital and McGill University.

1. Cavaré: Observation d'une paralysie général du sentiment et du mouvement affectant le type intermittent, Gaz. méd. de Toulouse **38**, 1853.
2. Hartwig, Hermann: Ueber einen Fall von intermittierender Paralysis spinalis, Inaug. Diss., Halle, 1874.
3. Holtzapple, G. E.: Periodic Paralysis, J. A. M. A. **45**: 1224 (Oct. 21) 1905.
4. Shinosaki, T.: Klinische Studien über die periodische Extremitätenlähmung, Ztschr. f. d. ges. Neurol. u. Psychiat. **100**: 564, 1926.
5. Herrington, M. S.: Successful Treatment of Two Cases of Familial Periodic Paralysis with Potassium Citrate, J. A. M. A. **108**: 1339 (April 17) 1937.
6. Singer, H. D., and Goodbody, F. W.: A Case of Family Periodic Paralysis with a Critical Digest of the Literature, Brain **24**: 257, 1901.
7. Biemond, A., and Daniels, A. P.: Familial Periodic Paralysis and Its Transition into Spinal Muscular Atrophy, Brain **57**: 91 (June) 1934.
8. Aitken, R. S.; Allott, E. N.; Castleden, L. I. M., and Walker, Mary: Observations on a Case of Familial Periodic Paralysis, Clin. Sc. **3**: 47 (July) 1937.
9. Ferrebee, J. W.; Atchley, D. W., and Loeb, R. F.: A Study of the Electrolyte Physiology in a Case of Familial Periodic Paralysis, J. Clin. Investigation **17**: 504 (July) 1938.
10. Allott, E. N., and McArdle, B.: Further Observations on Familial Periodic Paralysis, Clin. Sc. **3**: 229 (April) 1938.
11. Gammon, G. D.: Relation of Potassium to Family Periodic Paralysis, Proc. Soc. Exper. Biol. & Med. **38**: 922 (June) 1938.
12. Pudenz, R. H.; McIntosh, J. F., and McEachern, Donald: The Role of Potassium in the Mechanism of Family Periodic Paralysis, J. Clin. Investigation **17**: 530 (July) 1938.

the shoulder girdle and the upper and lower extremities. Weakness is occasionally hemiplegic in distribution at the onset but soon spreads to involve the opposite side. During severe attacks the patient is helpless and unable to make the slightest movement of the trunk or extremities. There is no disturbance of sensation.

Throughout the attacks he is depressed, irritable and uncommunicative and complains of headache, anorexia and nausea.

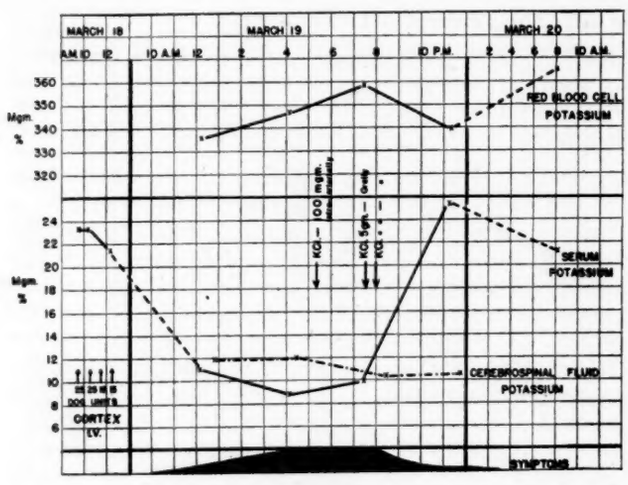

Chart 1.—Attack following adrenal cortex extract. The cerebrospinal fluid potassium did not alter with changes of serum potassium.

The pupils dilate widely and he is hypersensitive to light. The heart rate often drops to 40 beats a minute, and a systolic murmur develops at the apex. The skin is cool and the extremities are apt to be more moist than usual. The limbs are flaccid and the deep reflexes disappear while the superficial reflexes remain. During complete paralysis there is no muscular response to faradic or galvanic stimulation of nerve or muscle. Recovery of electrical reactions parallels the return to voluntary muscular power.

METHOD OF STUDY [13]

The patient was kept under observation for six months. Studies were made of eighteen separate attacks, of which eight were spontaneous and ten were induced. His intake of food and fluids and the collection of urine and stools were rigidly supervised. He received two standard diets which were alternated every three days. Expressed in grams, the two diets consisted of (*a*) protein 95, fat 68, carbohydrate 329 and potassium 3.73 and (*b*) protein 97, fat 110, carbohydrate 321 and potassium 3.93.

The potassium was checked by analysis of a duplicate diet. The sodium content was arrived at by calculation and the weighing of additional sodium chloride consumed. There was some variation of fluid intake as the result principally of the anorexia induced by the attacks, but at no time during the course of the experiment did the patient fail to consume the outlined diet. The urine was analyzed for potassium, sodium and chloride and the feces were analyzed for potassium. The urine was collected in twenty-four hour periods, save during the attacks when determinations were made in six or twelve hour periods. Stools were analyzed in periods representing three days of excretion. Standard methods were used for the chemical determinations. Potassium was estimated by the method of Kramer and Tisdall.[14]

METABOLIC STUDIES

Potassium.—Blood Serum and Corpuscles: There was invariably a marked fall of serum potassium during the paralytic phase both in induced and in spontaneous attacks (charts 1 and 2). These values ranged from 7.7 to 12.4 mg. per hundred cubic centimeters during complete paralysis. In one induced attack a value as high as 17.4 mg. was found during almost complete paralysis. The critical level in our patient was therefore variable. With improvement of muscular power the serum potassium rose again toward normal. There was also considerable variation of serum potassium during the interval phase. It ranged from 17.5 to 30 mg. per hundred cubic centimeters, although it usually lay between 22 and 25 mg. In the case studied by Aitkin and his associates,[8] onset of paralysis occurred when the serum potassium fell to 12 mg. per hundred cubic centimeters. A patient studied by Allott and McArdle [10] showed weakness whenever the level fell below 16 mg. per hundred cubic centimeters. Determinations of corpuscular potassium were made during two attacks. The serum was separated immediately after the blood samples were drawn. We are not able to interpret the variations of potassium in the blood cells (charts 1 and 2).

Intake and Output: Despite a constant intake of potassium, the excretion varied quite markedly from day to day. However, at no time was there any evidence of a positive or negative potassium balance over a representative period. During attacks there was a marked decrease in the excretion of potassium in the urine (chart 3), especially in the six hour specimens representing the phases of most marked paralysis. This was independent of urinary volume. A compensatory

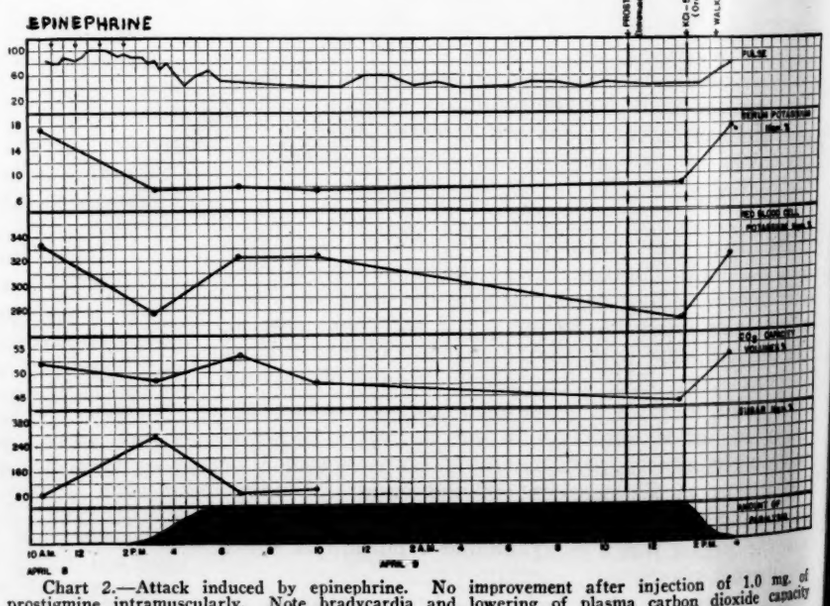

Chart 2.—Attack induced by epinephrine. No improvement after injection of 1.0 mg. of prostigmine intramuscularly. Note bradycardia and lowering of plasma carbon dioxide capacity during attack. Recovery after potassium chloride (5 Gm.) orally.

13. Miss Constance Lambertus supervised the nursing and Mrs. Ruth Salter and Miss Doris Brophy made the chemical determinations.

14. Kramer, B., and Tisdall, F. F.: Clinical Method for Quantitative Determination of Potassium in Small Amounts of Serum, J. Biol. Chem. **46**: 339 (April) 1921.

increase of output followed attacks. The first two attacks pictured in chart 3 were terminated by administration of potassium. The potassium content of the feces was variable but the total amount excreted was insignificant when compared to the urinary amount.

Cerebrospinal Fluid: During one attack the potassium content of the cerebrospinal fluid was determined

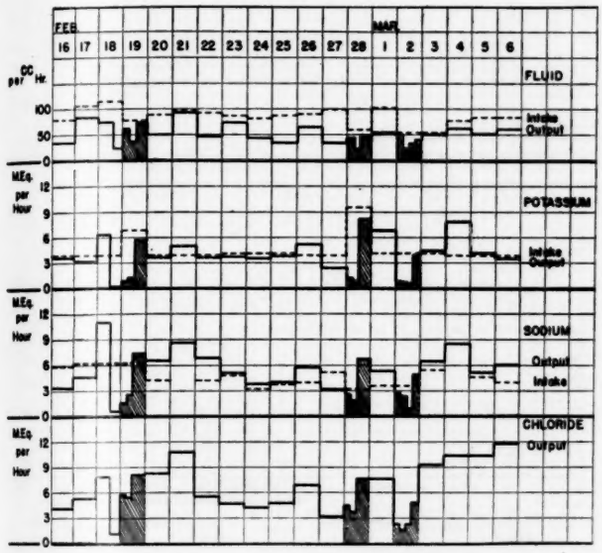

Chart 3.—Daily intake and urinary output of fluid, potassium, sodium and chlorides. The output of potassium, and to a lesser extent of sodium, is decreased on the days of the attacks. The latter are represented by the shaded areas. No diuresis of potassium preceded attacks.

on four different samples, representing stages from paralysis to almost complete recovery (chart 1). The values obtained varied from 10.3 to 12 mg. per hundred cubic centimeters, all of which were within the normal range of from 10 to 14 mg. There was no decrease corresponding to the lowering of serum potassium. The determinations covered a period of twelve hours, which seemed ample time for a change to become evident if it was going to occur. A specimen of cerebrospinal fluid obtained during the interval phase contained 11.6 mg. of potassium per hundred cubic centimeters.

Range of Level of Inorganic Phosphate, Calcium and Sodium in Blood Serum

	During Intervals, Mg. per 100 Cc.	During Attacks, Mg. per 100 Cc.
Serum inorganic phosphate	3.62- 4.75	2.74- 4.75
Serum calcium	10.4 - 11.8	10.1 - 11.4
Serum sodium	326.0 - 386.0	335.0 - 388.0

Other Electrolytes.—The urinary excretion of both sodium and chloride (chart 3) showed a slight decrease during the paralytic phase, followed by a compensatory increase during and after recovery. In the blood, the level of other important electrolytes was normal or without constant change during attacks. The range of numerous determinations is shown in the accompanying table.

Plasma Carbon Dioxide Capacity.—The carbon dioxide combining power of plasma was reduced moderately but consistently during attacks. Values obtained during two uninduced attacks were 50.4 and 52.9 volumes per cent. In one attack, induced by epinephrine, six values were obtained which varied from 43.5 to 53.7 volumes per cent. All values obtained during the interval phase have been above 64.4 volumes per cent.

Creatine and Creatinine.—Studies of creatine and creatinine in the blood and urine both during the attacks and in the interval phase have shown two definite abnormalities: (*a*) excretion of creatine in amounts up to 0.65 Gm.. in twenty-four hours and (*b*) a highly variable daily excretion of creatinine, the range being from 0.78 to 2.13 Gm. in twenty-four hours. These abnormalities bore no constant relationship to attacks (chart 4). The blood creatine and creatinine have always been within normal limits (chart 5).

Sugar.—Numerous determinations of plasma dextrose have fallen within a normal range or within the range of expectation following administration of dextrose, insulin and epinephrine. When attacks have been induced by those substances the fall of serum potassium has not been related to hyperglycemia or hypoglycemia (charts 2 and 6).

Choline Esterase.—Determinations of acetylcholine esterase in defibrinated blood and in serum were made by the method of Ammon.[15] The activity of this enzyme was not abnormal either during or between attacks. The mean values for five determinations on serum made during attacks and five made during intervals were 50.4 cubic millimeters of carbon dioxide and 48.4 cubic millimeters of carbon dioxide respectively. These results are well within the range found for a large number of normal persons.

PRODUCTION OF ATTACKS

Spontaneous attacks were infrequent and attempts were made to induce them. We enjoyed fair but not invariable success with epinephrine, ephedrine, large doses of dextrose or dextrose combined with either insulin or epinephrine. The success of these measures must depend on the natural cycle of the disease at the time they are applied. In addition, frequent attempts to induce attacks seemed to lead to a refractory state; thus, four times in one week the administration of 200 Gm. of dextrose failed to produce an attack. Repeated use of the other substances led to similar failures.

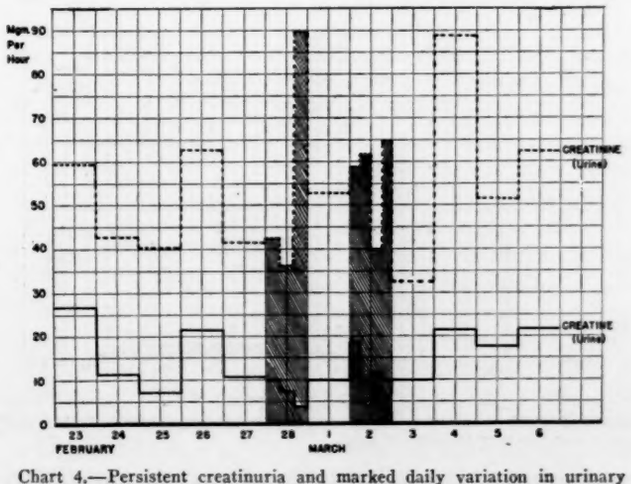

Chart 4.—Persistent creatinuria and marked daily variation in urinary creatinine. Shaded areas represent days of attacks.

Dextrose was given orally in amounts of from 200 to 250 Gm. at from 10 to 11 p. m. or in the early morn-

15. Ammon, R.: Die fermentative Spaltung des Acetylcholins, Arch. f. d. ges. Physiol. **233**: 486, 1933.

ing. If paralysis occurred it developed within three or four hours. Sometimes paralysis was incomplete. Twice, when no paralysis developed, administration of 1 cc. of epinephrine at hourly intervals led to paralysis within two hours of the first injection. On one occasion the combined use of insulin and dextrose led to a typical attack.

Epinephrine was given subcutaneously in 1 cc. (1 mg.) doses at hourly intervals. The sum total on any one occasion was 5 cc. If paralysis was forthcoming it tended to appear within two or three hours of the first injection. Ephedrine sulfate 1½ grains (0.1 Gm.) was given each hour by mouth. The results were similar to those obtained with epinephrine. On one occasion paralysis developed within one hour of the first dose.

Adrenal cortex extract was tried on two occasions because of its ability to decrease sodium and increase potassium excretion. The first time 50 dog units of Connaught Laboratory extract was given. The second time 80 units was given intravenously, as described by Thorn and his associates.[16] Each time paralysis developed on the day following the test. These experiments were inconclusive in that (*a*) chemical studies failed to demonstrate any increase in urinary potassium following administration of adrenal cortex extract, (*b*) dextrose was also given prior to one of the attacks.

The lowering of the alkali reserve during attacks led to an attempt to induce paralysis by acidosis. Seven hundred grains (45 Gm.) of ammonium chloride was administered orally over a period of four days. The carbon dioxide combining power fell from its initial level of 69 volumes per cent to 35.9 volumes per cent but the serum potassium remained quite stable, at no

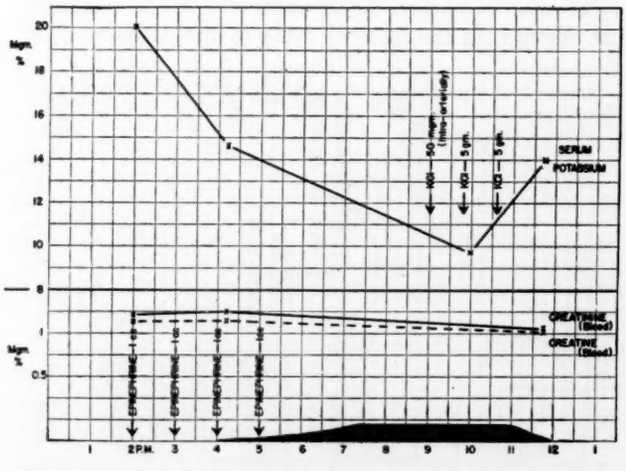

Chart 5.—Attack following epinephrine. Plasma creatine and creatinine remained stable. Injection of potassium chloride into brachial artery did not cause recovery in injected limb.

time falling below 17.9 mg. per hundred cubic centimeters. Slight weakness appeared in the back and the legs on the fourth day but no paralysis ensued.

No success followed an attempt to "wash out" potassium by large amounts of physiologic solution of sodium chloride intravenously, nor did lowering of the body temperature from 99.2 to 96.4 F. in a cold bath or taking severe and prolonged exercise lead to attacks.

16. Thorn, G. W.; Garbutt, H. R.; Hitchcock, F. A., and Hartman, F. A.: Effect of Cortin on Renal Excretion of Sodium, Potassium, Chloride, Inorganic Phosphorus and Total Nitrogen in Normal Subjects and in Patients with Addison's Disease, Endocrinology **21**: 213 (March) 1937.

ALLEVIATION OF PARALYSIS

Potassium.—Administration of potassium has invariably resulted in prompt disappearance of the paralysis. We have used potassium chloride most often, but the citrate is equally effective, although somewhat larger doses are necessary to provide an equivalent amount of potassium.

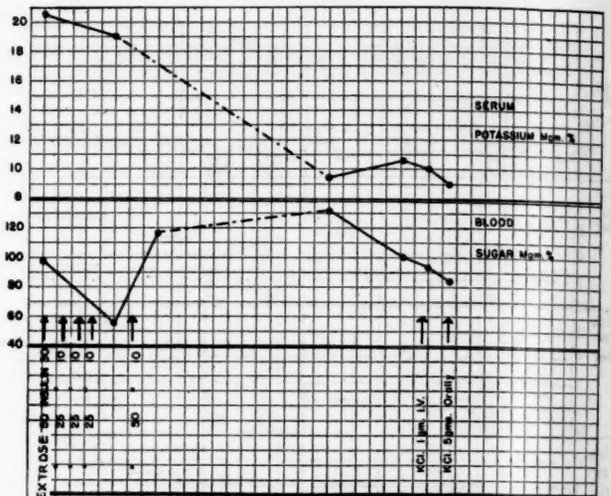

Chart 6.—Attack after dextrose and insulin. Lowering of serum potassium was not associated with hypoglycemia. Potassium chloride 1 Gm. intravenously caused partial recovery without elevation of serum potassium.

Potassium chloride, from 5 to 10 Gm. in watery solution by mouth, brought about return of movement within thirty minutes to one hour and the ability to walk unaided within two hours. Recovery was associated with a progressive rise of serum potassium (charts 1 and 2). Intravenous injection of potassium chloride caused much more rapid and dramatic recovery, the only disadvantage being intense burning pain along the course of the vessel even when the salt was injected in a concentration as low as 0.5 per cent. We usually injected 50 cc. of 2 per cent solution (1 Gm. of potassium chloride) during the course of ten minutes or less and did not exceed this amount. Severe thirst and cardiac extrasystoles sometimes occurred, but they disappeared when the injection was complete. Movement began to return in the limbs from four to eight minutes after the injection was begun, and the patient was able to stand within thirty minutes.

In his most severe attack the patient was almost unconscious and artificial respiration was necessary. Even the last rites of the church had been administered. Twenty minutes after the intravenous injection of 1 Gm. of potassium chloride the patient was sitting up and chatting. This amount was insufficient for complete recovery, however, and a further dose of the salt was given by mouth.

Since his discharge from the hospital four months ago, the patient has returned to full activity and has remained free from attacks. This has been achieved by the ingestion of 5 Gm. of potassium chloride each night as a prophylactic measure. Attacks had been occurring almost weekly prior to admission.

Choline Esters.—Acetyl-β-methylcholine chloride (mecholyl) 25 mg., was injected intra-arterially on two occasions. Movement became perceptible in the limbs within eight minutes and progressed to complete recovery. Choline chloride carbamate (doryl) 0.25 mg. was injected during two attacks, once intravenously and

once intra-arterially. Generalized movement commenced in four minutes on each occasion and progressed to complete recovery. Complete recovery thus occurred within two or three hours in all four instances without administration of potassium, while the serum potassium rose to the normal level as muscular power improved (chart 7).

In all experiments atropine, from 1/75 to 1/50 grain (0.0009 to 0.0013 Gm.), was given prior to the choline esters to reduce unpleasant side effects. Atropine itself had no effect on the attacks save for the fact that it caused the heart rate to increase from about 40 to 120 a minute, showing that the bradycardia was of vagal origin.

Other Drugs.—Prostigmine methylsulfate was administered intramuscularly during four attacks..

On one occasion after 0.5 mg. there was steady improvement for an hour and a half and the patient could walk. The effect wore off after three hours and paralysis returned. A temporary but less marked improvement occurred another time following 1 mg. On the third occasion 1.5 mg. of prostigmine was without effect. In one attack the drug was given after potassium had been administered and recovery was much more rapid than with potassium alone. The drug seemed capable of potentiating the recovery mechanism but obviously did not supply the mechanism itself.

Ergotamine tartrate had no effect on the paralysis.

MECHANISM OF ATTACKS AND SITE OF ACTION OF POTASSIUM

The foregoing results show that paralysis is associated with a redistribution of potassium between the blood and the body tissues. It was at first suspected

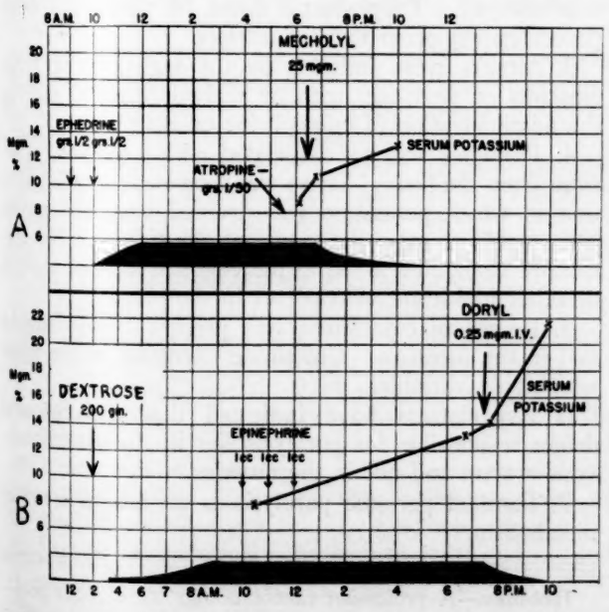

Chart 7.—*A*, attack induced by ephedrine and terminated by intra-arterial injection of mecholyl. *B*, attack induced by dextrose and epinephrine. Recovery followed 0.25 mg. of doryl intravenously. (Note the rise in serum potassium during recovery following injection of these choline esters.)

that the attacks developed because of abnormal loss of potassium from the body—a kind of potassium debt. This was disproved by balance studies. No undue loss of potassium preceded the attacks, and during the attacks excretion of potassium was greatly diminished. Indeed spontaneous recovery had often occurred without dietary or other sources of potassium, and this argued against depletion of the body's potassium stores.

During attacks the serum yielded its potassium to supply the demands of the tissues. On several occasions 1 Gm. of potassium chloride was given intravenously, improvement was rapid and the patient was walking within thirty minutes. During such partial recovery the serum potassium remained low, however, indicating that the injected potassium was leaving the serum and going elsewhere (charts 6 and 8).

Where then did the lack of potassium operate to produce paralysis and where did injected potassium remedy

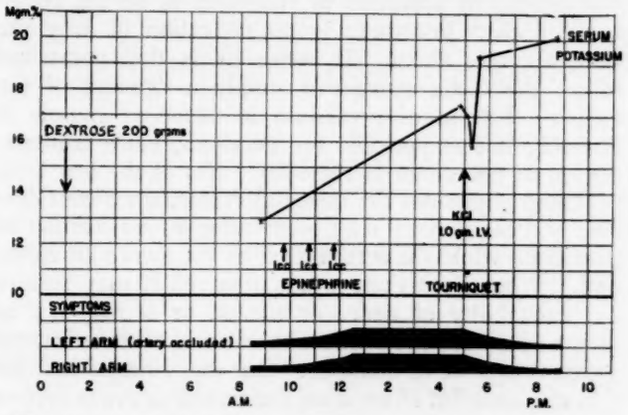

Chart 8.—Attack induced by dextrose and epinephrine. Potassium chloride injected into the right brachial vein. Note recovery of left arm despite arterial occlusion by tourniquet. The injected potassium rapidly disappeared from the blood serum. Serum potassium rose later during more complete recovery.

the defect? The distribution of paralysis and the loss of electrical excitability of the muscles pointed to a fault in the muscles themselves. On one occasion 20 cc. of potassium chloride in 0.5 per cent solution was injected into the left brachial artery while the venous return was obstructed for eight minutes by a blood pressure cuff inflated to 60 mm. of mercury to confine the potassium to the limb. Severe pain and intense vasoconstriction followed by flushing showed that the potassium had spread throughout the limb, but there was no recovery of power in the muscles. This amount of potassium chloride (0.1 Gm.) was theoretically sufficient to cause some local recovery, since as little as 0.5 Gm. had caused general improvement when injected intravenously in previous attacks. A negative result was obtained another time when 0.05 Gm. of potassium chloride was injected into the femoral artery.

These results suggested that the curative action of potassium was central or that some other substance was formed in the viscera by the action of potassium and thence carried to the muscles to restore their contractility. This led to the trial of certain choline esters as previously described. Intra-arterial injection of these substances caused no local recovery of power in the injected limb but when they entered the general circulation prompt recovery occurred throughout the body. We have no explanation at present for this action of the choline esters unless perhaps they stimulate some organ or tissue to release stored potassium.

From the following experiment (chart 8), which has been repeated three times with similar result, we are forced to conclude that the defect responsible for paralysis lies in the central nervous system: The arterial supply to one arm was occluded for from thirteen to seventeen minutes by a blood pressure cuff inflated to 200 mm. of mercury, while potassium chloride (50 cc. of a 2 per cent solution) was injected rapidly into the vein of the opposite arm. Movement began to return

in about five minutes in all limbs and recovery was as rapid in the still occluded limb as in the others. In other words, recovery occurred in a limb which was completely isolated from the rest of the body as regards humoral channels. These observations indicate that the defect is neurogenic. We have no explanation for the loss of direct electrical excitability of the muscles on this basis.

COMMENT

In the patient with familial periodic paralysis the relationship of paralysis to reduction of serum potassium is clear but there is no indication of why the change comes about. It seems likely that potassium leaves the blood stream to supply a demand of the tissues. Excess of potassium in nerve or muscle is probably not responsible for paralysis, since administration of potassium is remedial. Nor is the low level of serum potassium the essential factor, since considerable partial recovery may occur after administration of potassium while the serum level as yet shows no elevation. When potassium is administered it may restore the excitability of nerve or muscle or it may act as intermediary for the production of some other substance which is capable of doing so. Our experiments indicate that the remedial effect is on the central nervous system and not on the muscle directly. Spontaneous recovery or that following administration of choline esters suggests that some organ or tissue is capable of releasing sufficient potassium to rectify the needs of the inexcitable nerve or muscle and also to raise the serum level to normal.

The experiments of Allott and McArdle [10] indicate that in addition to undue lability of serum potassium some abnormality of the neuromuscular mechanism is present in this disease. They have succeeded in reducing the serum potassium to 10.5 mg. per hundred cubic centimeters in normal persons and have observed a level as low as 7.6 mg. in one person. In no instance was there paralysis. There is support for this in the abnormality of creatine metabolism described by Ferrebee, Atchley and Loeb [9] and by us. In our case there was persistent creatinuria even between attacks, and creatinine excretion was variable. Allott and McArdle found alterations of phosphorus metabolism paralleling those of potassium, and Milhorat [17] noted a negative phosphorus balance following attacks.

The fact that family periodic paralysis has been found to be an inborn error of metabolism should stimulate work on other hereditary diseases of the neuromuscular system which are at present looked on with such pessimism. It is of interest that the distribution of affected muscles in this disease is the opposite of that in myasthenia gravis and is similar to that seen in the myopathies. Biemond and Daniels [7] observed that in some patients with familial periodic paralysis an atrophy of the muscles most affected by paralysis developed in later life.

It is possible too that the condition may exist in minor forms which do not lead to complete paralysis. Shinosaki [4] was of the opinion that attacks of sudden weakness in the legs occurring in some patients with exophthalmic goiter (so-called Basedow's paraplegia) were minor examples of periodic paralysis. In view of the effect of insulin on serum potassium it would also seem advisable to test this possible mechanism in the rare monoplegias and other neurologic phenomena which do not respond to dextrose in cases of insulin shock. With the cooperation of Dr. T. E. Dancey we have determined the serum potassium in four patients receiving shock treatment for schizophrenia. Blood was taken before administration of insulin and again after from one and one-half to two hours of hypoglycemic coma. There was no significant change in serum potassium. These were patients, however, who recovered rapidly after the administration of dextrose and there were no persisting neurologic defects.

It is not possible to say whether the abnormality of potassium metabolism is peculiar to this disease or whether it is an exaggeration of a normal mechanism. Sodium metabolism appears to be unaffected and the defect is therefore unlike that of adrenal cortical activity.

The age incidence of the disease, its periodic character and its relation to thyroid activity all suggest an endocrine upset. At present, however, no gland or hormone is known to have so direct a relationship to potassium metabolism, and the primary cause of the disease must await further investigation.

SUMMARY

1. In a classic case of familial periodic paralysis, attacks were associated with a marked fall of serum potassium. During recovery the serum potassium rose to normal.

2. Administration of potassium caused rapid disappearance of paralysis. Acetyl-β-methylcholine chloride (mecholyl) and choline chloride carbamate (doryl) also brought about recovery, although no potassium was administered. Prophylactic doses of potassium have prevented the occurrence of attacks.

3. Attacks were induced by the ingestion of large amounts of dextrose, with or without insulin, and by the administration of epinephrine or ephedrine.

4. Paralysis was not associated with a loss of potassium from the body. There was, however, a redistribution in which potassium was drained from the serum presumably to meet the needs of the tissues. No significant change occurred in the concentration of sodium or other important electrolytes in the blood.

5. Persistent creatinuria was present during attacks and in the intervals. Creatinine excretion in the urine was highly variable.

6. Experiments have indicated that the chemical defect responsible for paralysis lies in the central nervous system and not in the muscles.

7. Familial periodic paralysis is an inborn error of metabolism.

17. Milhorat, A. T.: The Metabolism of Phosphorus in Periodic Family Paralysis, J. Clin. Investigation **16**: 676 (July) 1937.

Hobbies.—A profession cannot occupy all of one's time—or it ought not to—lest one become lopsided. Hobbies fill a gap in the lives of those who are most well rounded and promise equal satisfactions for less complete lives. . . . If you can grow, if you can relax, if you can be stimulated and refreshed by your hobby-tonic, you probably have found the right one. If you have not yet found it, begin thinking about it now, remembering meanwhile that Omnipotence of Thought isn't as efficacious as it once was, and that the surest way to develop an interest in a hobby is not by thinking about it but by doing something about it. You may be surprised how far it will take you. Hobbies cannot be developed on command. They develop by stages and are truly an expression of your very self.—Anderson, Camilla M.: Emotional Hygiene, Philadelphia, J. B. Lippincott Company, 1937.

STUDIES ON THE MECHANISM OF THE ACTION OF SULFANILAMIDE

I. THE BEARING OF THE CHARACTER OF THE LESION ON THE EFFECTIVENESS OF THE DRUG

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NEW YORK

The original observations of Domagk [1] on experimental mouse peritonitis and the clinical observations reported by Schreus [2] using prontosil (the disodium salt of 4-sulfamido-phenyl-2′-azo-7′-acetylamino-1′-hydroxynaphthalene-3′,6′ disulfonic acid) in the treatment of erysipelas led to the present investigations in April 1935. We have been interested, first, in evaluating the effectiveness and the limitations of this chemotherapeutic agent and its derivatives; second, in determining its mode of action, and, third, in throwing light on the biology of the hemolytic streptococcus. During the course of this study an increasing number of clinical reports have appeared; the effectiveness of sulfanilamide in certain infections needs no confirmation. The present report concerns itself primarily with an attempt to determine the mode of action on a number of bacterial infections encountered in a general hospital.

The published reports on the mode of action of sulfanilamide have in most instances dealt with observations in vitro or with a single type of experimental infection, peritonitis in the mouse,[3] and empyema in the rabbit.[4] Recently Osgood has added observations on culture of bone marrow.[5] It seemed to us that a study of the drug's effect on various types of hemolytic streptococcus diseases as they occur in man might lead to a hypothesis which could then be subjected to experimental tests. In this report the observations are chiefly clinical. Further experiments on the action of sulfanilamide in vitro will be reported shortly by one of us (J. S. L.).

GENERAL PROCEDURE

The present observations are drawn from the first 250 patients (1936 and 1937) treated with sulfanilamide in the various services of the Presbyterian Hospital-Columbia University Medical Center and Willard Parker Hospital. Each infection was identified bacteriologically. Each patient was seen daily by at least two of us. Sulfanilamide levels of the blood were followed in most cases. The dosage was regulated to maintain in the blood a minimum level of 50 micrograms when practicable. Uncombined sulfanilamide was quantitatively determined in the blood and other body fluids according to the method of Fuller.[6] Colorimetric comparisons against known standards were made in a stuphophotometer, color filter 530 being used. The drug was administered at intervals of either four or six hours, chiefly by mouth. Infections treated included those caused by the hemolytic streptococcus, meningococcus, gonococcus, Streptococcus viridans and pneumococcus. The diseases treated in the order of frequency were scarlet fever, tonsillitis, sinusitis, otitis, mastoiditis, lymphangitis, erysipelas, pneumonia, bacteremia, endocarditis, primary peritonitis, lymphadenitis, chronic surgical infections with draining sinuses, early abscess formation, cellulitis, infected diabetic gangrene, meningitis, puerperal fever and cutaneous infections.

TOXICITY OF SULFANILAMIDE: NO RELATION TO THERAPEUTIC EFFECT

At the beginning of this study the only toxic effect that had been reported was cyanosis.[7] We soon encountered a great many other toxic manifestations. Many of these have since been reported by other observers. All symptoms and signs referable to sulfanilamide toxicity were carefully recorded and an attempt was made to determine their possible relation to the effectiveness of the drug. Approximately half of the adults and one fifth of the children showed some toxic manifestations. Some of these have been mild and others alarming; however, none of the five deaths in this series of 250 cases resulted from drug toxicity. The toxic manifestations observed were (*a*) mild—cyanosis, symptoms of the gastrointestinal tract and of the central nervous system, fever, precordial and abdominal pain, and acidosis; (*b*) severe—rash, jaundice, anemia, hemoglobinuria, and granulocytopenia; (*c*) secondary reactions and late manifestations.

MILD MANIFESTATIONS

A. *Cyanosis.*—The development of cyanosis in patients receiving sulfanilamide has been a common occurrence. It was noted in approximately 50 per cent of adults and 20 per cent of children in whom the drug was used. This manifestation usually began with pallor and progressed to deep cyanosis, especially marked in the lips. In some persons cyanosis developed within twelve hours; most persons became blue before the third day of drug therapy. The intensity of the color seems to depend on the amount of drug in the circulation rather than on the amount of drug administered; it was paralleled closely by the concentration of methemoglobin in the blood as measured by the spectrophotometer (an illustrative case is given in the table). Cyanosis was detectable when the methemoglobin of the blood reached a concentration of 5 per cent and was striking at about 15 per cent. The highest value obtained was about 25 per cent in extreme cyanosis. Even at these levels there were no symptoms attributable to the methemoglobinemia per se. This manifestation did not seem to be dangerous in most cases, since it disappeared rapidly following withdrawal of the drug. However, in patients with diseases accompanied by lowered arterial oxygen, either systemically or in a localized area, the question arises whether the development of methemoglobinemia may aggravate the underlying disease. This problem has presented itself in pneumonia, in cardiac insufficiency and in recovery of compromised tissues following local inflammation or injury.

The work reported in this communication was conducted under the W. K. Kellogg Foundation Fund.

From the Departments of Surgery and Medicine, Columbia University College of Physicians and Surgeons, and the Presbyterian Hospital.

The authors are indebted to the Willard Parker Hospital and Dr. John Lyttle for the cases of scarlet fever. Dr. A. R. Dochez initiated this study and has given invaluable advice.

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2. Schreus, H. T.: Deutsche med. Wchnschr. **61**: 255 (Feb. 15) 1935; also personal communication to the authors.
3. Levaditi, C., and Vaisman, A.: Compt. rend. Acad. d. sc. **200**: 1694 (May 13) 1935. Nitti, F., and Bovet, D.: Compt. rend. Soc. de biol. **119**: 1277, 1935. Colebrook, Leonard and Kenny, Meave: Lancet **1**: 1279 (June 6) 1936. Colebrook, Leonard; Buttle, G. A. H., and O'Meara, R. A. Q.: Lancet **2**: 1323 (Dec. 5) 1936. Bliss, Eleanor A., and Long, P. H.: Observations on the Mode of Action of Sulfanilamide, J. A. M. A. **109**: 1524 (Nov. 6) 1937.
4. Gay, F. P., and Clarke, A. R.: J. Exper. Med. **66**: 535 (Nov.) 1937.
5. Osgood, E. E.: Culture of Human Marrow, J. A. M. A. **110**: 349 (Jan. 29) 1938.
6. Fuller, A. T.: Lancet **1**: 194 (Jan. 23) 1937.
7. Colebrook and Kenny.[3]

B. *Gastrointestinal Symptoms.*—A great many disturbances in physiology of the gastrointestinal tract have occurred, especially among adults. Particularly frequent have been anorexia, nausea, vomiting and abdominal pain. Diarrhea has been severe in a few cases. Like cyanosis, these symptoms have disappeared rapidly when sulfanilamide therapy has been discontinued. This problem has been particularly acute in infants, in whom essential maintenance of nutrition has been made difficult by the severe anorexia, and persistent regurgitation has sometimes been displayed.

C. *Disturbances of the Central Nervous System.*—Dizziness and headache have been fairly common symptoms of sulfanilamide toxicity among adults. Mild personality changes, especially lightheadedness and depression, have been noted in many persons shortly after beginning the drug. A few have become disoriented and even maniacal.

All these symptoms have subsided rapidly when drug therapy was stopped. In cases in which the condition of the patient demanded, the drug has been continued in spite of the appearance of the aforementioned mild manifestations of toxicity. Reduction of the dosage by 25 per cent has generally sufficed to prevent the development of more severe symptoms.

Observations on Patient B. Z. (History in Text)

Date	Sulfanilamide, Gm.	Cyanosis	Per Cent Methemoglobin	Serum Sulfanilamide, Micrograms per Cc.	Hemoglobin per 100 Cc. Blood
3/ 2	1.4	0	..	..	.....
3/ 3	4.4	++++	..	..	.....
3/ 4	3.8	++++	17	70	12 Gm.
3/ 5	3.0	++	16.5	..	.....
3/ 6	3.0	++	16	..	.....
3/ 7	3.0	++	..	..	.....
3/ 8	3.0	++	13	..	.....
3/ 9	3.0	++	..	..	.....
3/10	3.0	++	9	40	.....
3/11	3.0	++	..	..	.....
3/12	3.0	++	9	22	.....
3/13	2.6	++	..	..	.....
3/14	2.6	+	..	..	.....
3/15	2.6	+	6	20	.....
3/16	2.6	+	..	..	.....
3/17	2.6	+	..	..	.....
3/18	2.6	±	..	..	.....
3/19	2.6	±	4	20	.....
3/20	2.6	±	..	..	.....
3/21	2.6	±	..	..	.....
3/22	2.6	±	..	..	.....
3/23	2.6	±	4	..	.....
3/24	2.6	±	Trace	26	9.6 Gm.

D. *Sulfanilamide Fever.*—The development of drug fever has been an especially puzzling problem. This manifestation, rare in children, has been a frequent occurrence in adults. Most persons in whom sulfanilamide fever developed experienced some of the symptoms mentioned along with the appearance of pyrexia. A few, however, had pyrexia without symptoms. We have seen three different types of febrile response to sulfanilamide. The most common of these was a slowly rising temperature, occurring after the fourth day of therapy, progressing by stages each day (up to 106 F. in some instances) and falling about twenty-four hours after the drug was stopped. In some cases the temperature became normal within twenty-four hours but in most instances after forty-eight hours. In a smaller group of patients high fever and chills developed about twenty-four hours after the institution of therapy. These patients seemed to have a low tolerance for sulfanilamide. A few who had previously experienced sulfanilamide sickness showed a "hypersensitive reaction" on subsequent administrations of the drug from one month to one year later. As little as 0.6 Gm. of the drug given to these "hypersensitive" subjects was sufficient to produce profound reactions within six hours, characterized by aches, chills, temperature spiking to 104 F., headache and leukocytosis as high as 30,000 per cubic millimeter.

E. *Precordial and Abdominal Pain.*—A few patients showed unexplained abdominal pains during the course of treatment, located chiefly in the upper quadrants. This occurred mainly in patients who were showing other evidence of toxicity from the drug, such as cyanosis or gastrointestinal complaints.

F. *Acidosis.*—One severe case of acidosis occurred in this series. Cessation of drug therapy was followed by prompt recovery.

None of the toxic manifestations discussed up to this point has seriously affected the outcome of the disease. Less frequent but much more severe are the following drug manifestations:

SEVERE MANIFESTATIONS

A. *Rash.*—In eight patients a maculopapular rash developed during or just after sulfanilamide therapy. The appearance was similar in all cases, resembling confluent measles. Any part or at times the entire body was involved. Itching was severe in some cases. The drug was stopped in each instance at the onset of rash because of the fear that continued sulfanilamide therapy might result in severe exfoliative dermatitis. The rash usually persisted for two days or longer, finally clearing completely.

B. *Jaundice.*—Two types of jaundice appeared; one a severe hemolytic jaundice, the other presumably a result of hepatitis. Although the jaundice subsided when the drug was discontinued, transfusions were necessary in some cases. Jaundice has been an extremely disturbing development; in view of the possibility of permanent damage to the liver, sulfanilamide was discontinued whenever it appeared. The jaundice was usually accompanied by secondary anemia.

C. *Anemia.*—Mild anemias developed in a number of cases, but it was not possible to determine with certainty whether they were due to the infection or to the drug. In a few patients, however, a severe hemolytic anemia seemed attributable to sulfanilamide. This occurred after only moderate dosage of the drug. The most intense were accompanied by icterus, the less severe by progressive anemia. In one case a large spleen and liver developed which subsided after transfusion and discontinuance of the drug. Transfusions were employed freely in anemia and seemed to counteract progression to some extent.

D. *Hemoglobinuria.*—In two patients on moderate doses of the drug hemoglobinuria developed shortly after sulfanilamide therapy was instituted. In one of these cases there was an alarming drop in the hemoglobin level.

E. *Granulocytopenia.*—Two patients, both females, had a depression of leukocytes following sulfanilamide therapy. In both these cases the infection may have been largely responsible for the granulocytopenia, and the part played by the drug cannot be accurately determined. In one instance the granulocytes disappeared completely and an alarming pyrexia developed. In both cases the final outcome was satisfactory.

SECONDARY REACTION: LATE MANIFESTATIONS

The drug symptoms mentioned up to this point usually appeared during the course of therapy. In one man severe sulfanilamide manifestations developed

eighteen days after the drug had been stopped, including pyrexia of 105 F., jaundice, enlargement of the spleen and liver, and a rash. It seemed perfectly definite that this patient had severe sulfanilamide sickness with hemolytic jaundice. The unusual feature was its appearance more than two weeks after the last dose of the drug.

The foregoing evidences of drug toxicity bore no observable relation to the effectiveness of sulfanilamide in overcoming infection. In some of the patients who showed marked toxic effects, the underlying infection seemed to be checked by the drug and promptly flared when the drug was discontinued. On the other hand, some patients who had toxic symptoms, such as severe cyanosis, were not benefited. The chief importance of the drug symptoms was their limiting effect on the amount of sulfanilamide that could be given. As far as the effect of sulfanilamide on the infectious agent was concerned, the presence or absence of symptoms of drug toxicity was irrelevant.

SEROLOGIC TYPE OF HEMOLYTIC STREPTOCOCCUS: NO RELATION TO EFFECTIVENESS OF SULFANILAMIDE THERAPY

It was not known whether all serologic types of hemolytic streptococci could be influenced by sulfanilamide or whether some were refractory to this drug. Daily cultures of the infected sites were made in most patients before, during and after chemotherapy was instituted. The organisms were typed according to the method described by Griffith.[8] Of the known types of hemolytic streptococci of group A, all but four were represented in this series. It was not possible to correlate the effectiveness of the therapy with the serologic type. No type seemed refractory to the drug. Moreover, human infections with organisms of Lancefield's groups C and G as well as group A seemed to be influenced by sulfanilamide therapy.

THE PROBLEM OF RELAPSE FOLLOWING WITHDRAWAL OF SULFANILAMIDE

The administration of sulfanilamide was followed in a high proportion of cases by the disappearance of the infectious agent from cultures and the subsidence of signs and symptoms. The infecting organism had apparently been destroyed. In many hemolytic streptococcus infections, however, organisms which had disappeared during the course of treatment reappeared in predominance or even in pure culture within seventy-two hours of the time the drug was stopped. In most instances this was of no clinical importance. In a number of patients, however, the reappearance of the organism was accompanied by relapse. This occurred mostly in patients who had received the drug for less than ten days.[9] It was also noted that relapses were more common in some diseases than in others. They were frequent in patients with localized infections containing necrotic tissue, such as mastoiditis and abscesses, whereas in bacteremia and erysipelas they were not encountered. A few illustrative examples are given:

Reappearance of Organism Without Symptoms.—Many patients whose cultures had become negative for hemolytic streptococci had a reappearance of organisms of the same serologic type in almost pure culture at the site of infection within three days after the drug had been stopped. This was particularly common in cases of acute pharyngitis and tonsillitis. In the majority of them convalescence proceeded uneventfully without return of fever or symptoms.

E. S., a boy aged 12 years, with mild scarlet fever, was given 2.5 Gm. of sulfanilamide a day for four and a half days. Culture on admission of material from the throat yielded predominantly the hemolytic streptococcus. Succeeding cultures showed the organism in decreasing numbers. After medication was stopped, the organisms began to increase rapidly. A week after the drug was stopped the hemolytic streptococcus was again predominant, and there was a mild temperature rise to 100.4 F. without symptoms.

Reappearance of the Organism with Mild Symptoms.—Some patients who showed a return of the infectious agent experienced mild symptoms of the same character but less severe than the original disease. These symptoms usually disappeared without administration of sulfanilamide being resumed. This was especially common in persons with throat infections but occurred also in other types of infections.

M. S., a woman aged 20, a student nurse with severe hemolytic streptococcus pharyngitis, was given sulfanilamide 4 Gm. for three days and 3 Gm. for two days. Culture of material from the throat the day medication was begun showed hemolytic streptococcus, type 13, predominating. Culture the day after medication was negative for the hemolytic streptococcus and continued so for a week. There was marked subjective improvement with a drop in temperature on the day following medication (perhaps coincident with rupture of an intratonsillar abscess). The patient was discharged from the hospital ten days after medication was stopped. On the same evening she had a recurrence of tonsillitis with cervical adenitis and a slight rise in temperature. Culture of material from the throat again yielded hemolytic streptococcus, type 13, predominantly.

Recurrence of Severe Disease.—In other patients a moderately severe disease picture developed, not unlike the original symptoms, when the drug was discontinued.

J. C., a woman aged 37, was admitted with chronic otitis and mastoiditis. Culture showed the hemolytic streptococcus. After four days in the hospital the temperature rose to 103 F. and frank signs of erysipelas developed about the ear. Sulfanilamide 4 Gm. a day was given and she showed marked improvement. The erysipelas disappeared and the temperature returned to normal. One week later she was being prepared for mastoidectomy and sulfanilamide was discontinued. After three days without the drug there was a recurrence of the erysipeloid lesion, mild fever, followed by edema of the eyelids and pain around the edge of the lesion. Sulfanilamide was again administered in the same doses and the response was similar to the original response; i. e., the temperature and cutaneous lesions disappeared in three days. The drug was continued, however, for nearly two weeks, at the end of which time no further relapse occurred.

The following cases show that patients with purulent lesions require a long course of therapy, owing to the survival of organisms in foci. In this group permanent clinical recovery seemed to depend on the development of adequate normal defenses. When this occurred, symptoms disappeared permanently, even in cases in which the individual remained a carrier of the infecting agent.

The first patient with a uterine infection required two weeks of chemotherapy before she was able to control the invasiveness of a virulent organism without the assistance of the drug.

M. C., a woman, had a postpartum infection, with a fever of 104 F. Vaginal culture showed the hemolytic streptococcus, group A, type 13, in pure culture. She was given sulfanilamide

8. Griffith, F.: J. Hyg. 34: 542 (Dec.) 1934.
9. The procedure subsequently adopted to prevent relapses has been to diminish the dose gradually over a period of days, the temperature curve being used as an index of controlled infection. Secondary courses of therapy were employed only when absolutely necessary, because of the greater incidence of severe toxic reactions in such cases.

2 Gm. the first day, and then 4 Gm. each day for one week. The temperature fell to normal within thirty-six hours. The sulfanilamide level of the blood at that time was about 30 micrograms per cubic centimeter. After one week the dosage was diminished to 2.6 Gm. Coincident with this the temperature rose, severe symptoms returned and cultures of material from the vagina became strongly positive with type 13. It was then necessary to increase the drug to the point of toxicity. The cultures of material from the vagina again became free of streptococcus when the sulfanilamide level in the blood reached 50 micrograms. After two weeks of therapy it was possible to discontinue the drug without untoward symptoms, although the patient remained a carrier for a period of months.

The next history likewise illustrates the necessity of maintaining a high level of sulfanilamide in the blood until natural resistance has had time to develop:

H. M., a young woman, was admitted to the hospital because of chills, fever and red and painful legs of twenty-nine hours' duration. On admission, the temperature was 105 F. and she showed massive edema with redness of the lower extremities and slight edema of the hands and face. There were large irregular tender blisters over the surface of the legs. It was felt that she had hemolytic streptococcus cellulitis, probably with infection of the blood stream, and sulfanilamide therapy was begun immediately. Blood culture on admission showed the hemolytic streptococcus in two flasks. Twenty-four hours after treatment the blood stream became sterile. However, cultures of the necrotic lesions on the legs were positive on the fourth day, when the blood contained 40 micrograms of sulfanilamide per cubic centimeter. The dosage was lowered on the eighth day. Three days later the temperature rose as the alarming symptoms returned and the dosage was again increased with prompt effect. It was possible to discontinue the drug during the fourth week without untoward results, although she remained a carrier.

So far as could be determined, sulfanilamide did not depress the development of the normal defense mechanism; but drug therapy was needed until the time of this development.

DEVELOPMENT OF METASTATIC LESIONS AND BACTEREMIA

In several patients hemolytic streptococcus metastatic lesions developed after the course of sulfanilamide therapy had been terminated, at a time when recovery was believed to be complete. In others hemolytic streptococcus bacteremia developed about thirty-six hours after the drug had been either stopped or markedly diminished in amount. In these cases the reduction in dose was prompted by the onset of mild toxic manifestations; the consequences of withdrawal were almost disastrous.

C. D., a girl aged 7 years, admitted with scarlet fever and signs of acute mastoiditis, was given sulfanilamide approximately from 2 to 3 Gm. each day. The temperature, which was 107 F. on admission, subsided slowly, keeping a range of about 100 to 101 F. In preparation for mastoidectomy, the dosage was lowered. Following mastoidectomy, the temperature rose markedly, reaching a height of from 105 to 106 F. Blood culture taken at this time showed hemolytic streptococcus of type 5, the same as the organisms recovered from the ears and throat on admission to the hospital. Sulfanilamide therapy was again started in similar doses and subsequent blood cultures all remained sterile. The temperature, however, spiked to from 103 to 104 F. for a number of days, and the patient remained acutely ill for two weeks following bacteremia. Eventually, on sulfanilamide therapy, the temperature subsided, and the patient was discharged fifty days after admission. This accident, almost fatal, followed the discontinuance of the drug.

These observations suggested that the protective action of sulfanilamide was greatest in the circulating fluids and that, after withdrawal, bacteria remaining in necrotic tissues could become highly invasive.

THE RELATION OF FREE SURGICAL DRAINAGE TO THE EFFECTIVENESS OF SULFANILAMIDE THERAPY

So far as could be determined, sulfanilamide was of no therapeutic value against well developed abscesses. In these cases surgical drainage later brought prompt relief.

We have encountered several chronic streptococcic infections refractory to surgical treatment in which the natural defense mechanism was not capable of preventing the occasional migration of organisms to new tissue. There was little immediate risk of generalized blood or lymphatic invasion, yet the antibacterial forces were not strong enough to overcome the infection. We present two cases of this type in which sulfanilamide proved highly effective. In the first case, one of long duration, the drug was continued well beyond the stage of healing, and the result was completely satisfactory, at least as far as one can judge from the follow-up period of eighteen months. In the second case, premature withdrawal of the drug following an initial satisfactory response was followed by the reappearance of streptococci in the exudates and a simultaneous flare-up in the activity of the local infection. Resumption of sulfanilamide therapy eventually cleared this infection.

M. S., a school girl aged 15 years, first admitted to the private pavilion under the care of Dr. Auchincloss Jan. 9, 1931, had had hemolytic streptococcus septicemia eleven months before, followed by pneumonia and suppurative arthritis of the right sacro-iliac joint. The latter had drained spontaneously at the right pelvic brim seven months before, and the discharge had continued intermittently ever since, inadequate drainage producing periodic spikes of fever.

Over a period of sixty-eight months, the patient continued to have almost constant suppuration in the pelvis. She had twenty-six operations during that time. It was found that constant maintenance of free drainage both anteriorly and posteriorly was essential in order to prevent the formation of new abscesses. The process later invaded the uterovesical space and produced an anterior vesical fistula, which finally closed. She either had drainage tubes constantly in place to prevent closure and backing up of pus, or else her ambulatory period was of short duration, an early recurrence of pain and fever bringing her back to the hospital.

Her last operation was on Oct. 13, 1936, when simple excision of a granulating tract in the lower anterior wall of the abdomen was done. Following the immediate postoperative period, her temperature became normal, but she continued to have fairly profuse drainage from each of three tracts, cultures showing the same type 13 (Griffith) hemolytic streptococcus which had constantly occurred in almost pure culture in her discharges.

Sulfanilamide 3 Gm. daily was started October 27 and continued until discharge November 23. The draining sinuses were irrigated with a 1.2 per cent solution of sulfanilamide in 0.5 per cent saline solution. The discharge diminished rapidly in amount after treatment was started and became thin and sticky, the granulations lining the sinuses assumed a healthy appearance, and the sinuses filled in rapidly from the depths. It appeared on purely clinical grounds to Dr. Auchincloss, who had had the patient under almost constant observation for five and a half years, that a type of healing was taking place which he had never observed in this patient's wounds. A follow-up period of eighteen months has now passed without any evidence of recurrent disease. After discharge from the hospital, she continued to take from 1 to 2 Gm. of sulfanilamide daily for about one month. At no time were serious symptoms or signs of toxicity noted.

L. B., a woman aged 26, a telephone operator, complained of ulceration of the pectoral region for ten months. At that time an abscess had developed in the right breast which had been incised and drained but failed to heal. Spreading and undermining continued in spite of repeated surgical procedures in

several hospitals. The patient had had some fever most of the time and a great deal of pain. On examination the patient was emaciated with extensive ulceration of the right pectoral region, the right breast being attached by only a short pedicle of skin beneath the clavicle. There was undermining of the skin peripheral to the ulcer, and three "daughter ulcers" had formed in the pectoral and infraclavicular regions. Exudate was profuse and foul. Cultures showed hemolytic streptococci.

With no operative intervention the patient was started on sulfanilamide 4.5 Gm. daily. After nine days the cultures showed no hemolytic streptococci and marked clinical improvement had occurred, so that the drug was stopped when the patient became nauseated. After six days without sulfanilamide there was an increase in the amount of discharge, the wound looked worse and cultures showed reappearance of streptococci. The drug was resumed and rapid improvement again occurred, although this time the disappearance of the hemolytic streptococci from the wound was slowed. During the next twelve weeks she continued to receive sulfanilamide, though most of the time the usual daily dose was only 2.5 Gm. During the fourteen weeks of hospitalization it was possible to perform a plastic operation, with excision of contracted scar tissue and resuture of the breast to the chest wall. This healed uneventfully and the patient was discharged.

Both of these chronic infections were treated successfully. In the presence of sulfanilamide the organisms were unable to form metastatic lesions. Free surgical drainage permitted elimination of pus. The combined treatment gradually eliminated the organisms, which had persisted deep in the wounds for a long time. In the first of these cases most of the necrotic tissue which might have served as a protected nidus for persistent infections had been surgically removed. In the second case there was little deep necrosis when treatment was started.

THE RELATION OF MIXED INFECTIONS TO THE EFFECTIVENESS OF SULFANILAMIDE THERAPY

In necrotic lesions in which both hemolytic streptococci and hemolytic staphylococci occurred, drug therapy was often ineffective even in the presence of free surgical drainage. The staphylococci in local lesions were not influenced by sulfanilamide. The continuation of purulent lesions with this organism seemed to inhibit the chemotherapeutic effect of sulfanilamide on hemolytic streptococci.

A. McL., a housewife aged 37, had an indolent infection of the interphalangeal joint of the left thumb which was observed for several days in the outpatient department. She was finally admitted for incision and drainage, at which time cultures from the joint space showed hemolytic streptococci. Sulfanilamide was started on the fifth day after operation in order to see whether rapid elimination of the streptococci could be effected. On the seventh day Staphylococcus aureus as well as streptococci was found in the exudate, and these two organisms persisted in the wound for three weeks in spite of continued sulfanilamide. Little effect on the character of the lesion was obtained by local irrigation with sulfanilamide solution.

The possibility suggested itself that the staphylococcic activity created environmental conditions which interfered with the effect of sulfanilamide on the streptococcus.

THE EFFECT OF SULFANILAMIDE ON RAPIDLY SPREADING INFECTIONS

Sulfanilamide therapy seemed most effective in rapidly spreading lesions in which there had been little tissue destruction:

J. I., a man aged 31, an apartment house superintendent, was admitted with extensive cellulitis of the left hand twenty-four hours after introduction of a splinter of manila rope into the middle finger. The temperature was 103 F. on admission. In spite of the very short time since the primary injury, there was a well developed pattern of lymphangitis extending to the shoulder. There was exquisite tenderness and swelling around the site of the splinter wound, but no signs of tenosynovitis were present. An exploration of the superficial layer of skin around the wound was made to see whether any foreign body was present, but incision of the closed spaces of the finger was not done because of the unlocalized character of the infection. Sulfanilamide was started, wet dressings and elevation were instituted and, within twenty-four hours, subsidence of spread of the lesion had definitely commenced. On the fifth day the temperature returned to normal. On that day, signs of localized abscess were noted and the middle closed space of the middle finger was incised. A small drop of pus was obtained which showed hemolytic streptococci. Further recovery and wound healing were uneventful. Blood cultures throughout were negative.

This patient recovered promptly from a dangerous infection. The therapeutic effect of the drug was striking in the newly invaded tissues; however, a small abscess which developed continued to yield viable organisms in spite of sulfanilamide therapy.

A second case illustrates the effectiveness of sulfanilamide in preventing invasion into the meninges and its inability to sterilize necrotic tissue:

C. S., a boy aged 4 years, was admitted to the Babies Hospital because of intermittent earache and headache for three weeks. On lying down he complained of pain in his head, which was relieved on sitting up. There was an extensive, soft, fluctuant, exquisitely tender swelling over the right parietal region over the occipital bone. The right tympanum was wihte and bulging posteriorly; surface vessels were prominent.

On the day of admission a right simple mastoidectomy was performed. Near the sinodural angle there was a collection of creamy pus. The dural plate and mastoid cells in this region were soft. Pus continued to appear in such a steady stream that it was necessary to remove an area of bone extending about an inch toward the occiput. The dura was shaggy, thickened and inflamed and the brain beneath was soft.

He stood the operation fairly well and was given a small transfusion afterward. The temperature reached 103 F. on the two following days. Culture of the pus from the epidural abscess showed a pure culture of hemolytic streptococcus. Sulfanilamide was begun on the second day after operation and continued for three weeks (2.5 Gm. a day).

On the fourth and fifth days he was afebrile, but the temperature began to rise at the end of the first week and continued elevated through the second week. A superficial incision at this time released more pus, and the temperature fell to normal. He continued afebrile during the fourth week, when sulfanilamide was stopped. He was discharged after six weeks.

At home he appeared to be well for a period of ten days, without fever or complaint. On the eleventh day he awoke at 1 a. m., feverish, complaining of headache. He was brought to the hospital and while in the clinic had a generalized convulsion lasting two minutes. He was readmitted with a temperature of 104 F. The previously operated area was explored for brain abscess; none was found. However, necrotic bone was removed from two sites; each contained a pure culture of the hemolytic streptococcus. Throughout the second admission he received 2.5 Gm. of sulfanilamide a day until the ninth week, when the dose was reduced to 2 Gm. He was discharged after nine weeks, having made a satisfactory recovery.

Sulfanilamide prevented further spreading of this dangerous infection but was unable to kill organisms in necrotic bone.

A third case shows that under some circumstances the use of sulfanilamide in a rapidly spreading lesion may lead to the formation of a sterile abscess:

B. Z., a school boy aged 16 years, was admitted with hemolytic streptococcus septicemia associated with pansinusitis. He was desperately ill, with a temperature of 105 F., and showed a diffuse cellulitis of the right temporal region. On the day of

admission signs of acute suppurative arthritis of the right shoulder developed. Under sulfanilamide therapy his blood became sterile within forty-eight hours. The signs of cellulitis of the temporal region subsided, leaving a localized, fluctuant area which, when opened, yielded sterile pus on repeated cultivation. The shoulder signs and symptoms disappeared without surgical intervention. The data are given in the accompanying table.

Sterile abscesses were found in two other patients treated with sulfanilamide. In all three cases treatment was instituted before localization had occurred. It appeared that sulfanilamide sterilized the lesions when administered before necrosis of the tissue had taken place.

Finally, another case illustrates the effectiveness of sulfanilamide in a rapidly spreading infection and its ineffectiveness in a localized lesion:

M. K., an infant aged 11 months, was admitted in the early stages of acute primary hemolytic streptococcus peritonitis with septicemia. Blood and abdominal paracentesis yielded a pure culture of the hemolytic streptococcus. Under sulfanilamide therapy the blood became sterile and the signs of peritonitis disappeared after one week. No localized peritoneal abscess formed.

During the second week a suppurative phlebitis developed around an infusion cannula in the saphenous vein, and coincident with this blood culture became positive. Because of suspected hepatitis, sulfanilamide was withheld for twenty-four hours and the colony count rose from 10 to 1,328 per cubic centimeter in the blood culture. Sulfanilamide therapy was resumed and an abscess which formed at the site of the phlebitis was drained. Examination of the pus showed hemolytic streptococcus in pure culture. The blood became sterile and remained so. Recovery was complete, and the patient has enjoyed good health during the follow-up period of fourteen months.

Sulfanilamide sterilized the blood stream and the peritoneal cavity in this critically ill infant. However, in the presence of traumatized tissue and hematoma formation sulfanilamide was unable to sterilize a localized infection. Organisms in this focus remained highly virulent but were unable to form metastatic lesions elsewhere in the presence of a high level of sulfanilamide in the blood.

SULFANILAMIDE THERAPY: NO EFFECT ON IMMUNE BODY FORMATION

That sulfanilamide may have toxic effects on the liver, spleen and bone marrow has been pointed out. Whether this drug might depress or stimulate antibody formation was unknown. To determine this, two types of studies were made.

The first of these consisted in serial determinations of antistreptolysin over a period of from thirty to sixty days after infection. This antibody to the streptococcus was examined because it permits quantitative measurement and because previous experience had indicated the normal curves in untreated infections. Samples of blood were obtained at intervals of from two to seven days, and the antibody curves for approximately 100 patients receiving sulfanilamide were determined. On the whole, the curves were similar to those of untreated patients.

The second study was made on guinea pigs. Serial determinations of antistreptolysin were made on animals given agar foci, inoculated with varying doses of hemolytic streptococcus, N Y 5 (0.0001, 0.1 and 0.5 cc. of eighteen hour broth cultures) and treated for varying periods (two, three and four weeks) with sulfanilamide (5 cc. of a 2 per cent solution twice daily). Thirty-two pigs were treated with sulfanilamide; eight controls were untreated. The hemolytic streptococcus was recovered from the abscesses of all pigs but one. In the treated pigs that survived for two weeks after infection, antistreptolysin levels developed similar to those in the controls. One control pig failed to form the antibody. There was no indication that sulfanilamide had any effect on production of antistreptolysin.

COMMENT

The clinical aspects of this study showed striking differences in the effectiveness of sulfanilamide. These differences were related more to the character of the lesion than to the identity of the bacterial infection. Sulfanilamide was most effective in bacteremia, lymphangitis, erysipelas and cellulitis; it was highly effective in early infections with little suppuration. It had a questionable effect in scarlet fever, tonsillitis, sinusitis, otitis and mastoiditis. The drug was ineffective when abscesses were well established, except perhaps in limiting their further spread and protecting normal surrounding tissues against invasion when drainage was used.

So far as could be determined from scarlet fever, the drug had no effect on toxemia of streptococcic origin. It is possible, however, that the symptoms in these persons were due to toxin absorbed before sulfanilamide therapy was instituted. The majority of strains of hemolytic streptococci showed little change in their production of hemolysin following sulfanilamide therapy. In a few organisms, however, production of hemolysin was strikingly inhibited. It seemed to us that any depression in the production of soluble toxins was of secondary importance.

The striking effect of sulfanilamide was a depression of the invasive properties of the organism. This effect was definite within eighteen hours in the case of bacteria circulating in tissue fluids or in newly invaded tissues.

In contrast, the presence of débris, human or bacterial, diminished the effectiveness of sulfanilamide on the hemolytic streptococcus. In each instance the organisms remaining in broken down tissue maintained their virulence. It is not known whether the débris itself had a protective action on the organisms or whether there was insufficient penetration of the drug into the locus.

It seems possible that sulfanilamide may alter the total metabolism of the micro-organism or may interfere especially with some specific function, such as its capacity to digest protein. In either case the presence of necrotic tissues appears to be of great importance. Sulfanilamide should be considered an agent which supplements, and in no way supplants, antibacterial immunity. These aspects of the problem are now under experimental investigation by one of us (J. S. L.) and will be the subject of a forthcoming report.

CONCLUSIONS

The effectiveness of sulfanilamide therapy is related to the type of lesion.

The function of the micro-organism, which is strikingly depressed by sulfanilamide, is its capacity to invade tissue.

The effect of the drug on bacterial invasiveness seems to be influenced by the amount of débris present in the lesion.

These phenomena are being investigated experimentally to determine the mode of action of sulfanilamide.

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PSEUDOHYPERTROPHIC MUSCULAR DYSTROPHY

AN EVALUATION OF RECENT STUDIES

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The treatment of pseudohypertrophic muscular dystrophy has passed through many cycles, depending on the prevailing theory of pathogenesis. Each has had a short period of usefulness which ended when failure to produce enduring clinical improvement made it no longer tenable. At present the myodystrophic patient will probably pass through the entire gamut of therapy, beginning with the more recent forms and working backward as each in turn is discarded as ineffective.

For a time all interest centered on endocrinologic factors,[1] and practically every gland was incriminated. The pineal and pituitary[2] glands were particularly singled out by many workers, who pointed to a similarity of symptoms in diseases of these ductless glands to those found in the dystrophic patient.

In medical writings repeated emphasis is placed on a supposed disturbance in carbohydrate metabolism.[3] These statements are based on chemical studies[4] and on deductions drawn from the occurrence of creatinuria in unrelated conditions such as diabetes and starvation.

Occasionally a sporadic case of pseudohypertrophic muscular dystrophy is reported occurring as a postencephalitic residuum or following acute anterior poliomyelitis.[5] This has led some writers to hypothesize a lesion in a hypothalamic center.

In 1930 Kuré and Okinaka[6] began treating their patients with epinephrine and pilocarpine, basing their therapy on the belief that the disease had its origin in a lesion of the autonomic nervous system. They reported very encouraging results, varying from startling improvement to a retardation or halting of the progress of the disease.

Hough and others in this country followed along these lines and reported good results. Our experience with this form of therapy has been disappointing.

Beginning with the work of Milhorat, Techner and Thomas[7] in 1932, the literature was studded with enthusiastic reports on the use of aminoacetic acid in the treatment of the primary myopathies, particularly pseudohypertrophic muscular dystrophy and myasthenia gravis. Along with Tripoli and Beard,[8] Boothby[9] and others, we too obtained encouraging results. As our experience with amino acid therapy progressed, however, it became apparent to us that the progress of the disease remained unaltered and that temporary improvement, if any, was short lived in the face of advancing atrophy and fibrosis.

Our interest was again revived on learning of the recent work of Meldolesi[10] in Italy, covering a period of nine years and based on more than 100 cases. The theory advanced by this worker is that the muscular dystrophies are caused by a primary disease affecting the pancreas, as a result of which tryptic and lipolytic digestive processes are markedly impaired. Failure of adequate protein absorption causes a depletion of protein reserves resulting in a dysplasia of striated muscle. This occurs in persons showing a hereditary and familial diathesis the basis of which is a lack of pigment of the muscles.

More specifically Meldolesi reported that the curves for the secretion of lipase, diastase and trypsin were delayed in their rise and did not reach normal levels. Many patients showed a diminished dextrose tolerance. The feces contained an increased amount of neutral fats and fatty acids. The urines showed a total excretion of nitrogen which was low and independent of the intake of protein before therapy was started and showed a rapid rise under treatment. Following the institution of therapy, creatinuria rapidly diminished until within a few weeks a negligible amount was excreted. Similarly the excretion of creatinine increased in a rapid progressive way until it made up almost the whole fraction of the total creatinine. Treatment was directed toward correcting the deficient digestion of protein and altered carbohydrate metabolism.

Meldolesi's treatment was essentially the administration of from 40 to 60 drops of pepsin-pancreatin (a product of Richter of Budapest) twice a day, insulin and intravenous dextrose.

In the present work we attempted to determine the soundness of several of Meldolesi's basic contentions, namely:

1. That these patients are unable to digest proteins because of a lack of or deficiency in their tryptic ferments.
2. That, because of this deficiency, excretion of urinary nitrogen is independent of variations in the intake of protein nitrogen.
3. That these patients have a disturbed carbohydrate metabolism as evidenced by a diminished tolerance for dextrose.
4. That creatinuria is progressively abolished following institution of therapy.

MATERIAL AND PLAN FOR THIS STUDY

A small group of patients was admitted to the Max Pam Unit for Metabolic Research, where they could be studied intensively under controlled conditions. This seemed to us more desirable than ordinary hospitali-

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zation of a larger group, in which the amount of study would be necessarily restricted.

Five patients were selected, each of whom had been under observation for several years and had passed through the gamut of the more recent forms of therapy. Two of these patients were typical examples of the Duchenne type. Two belonged to the same group but presented a variant in the form of a superimposed Froelich's syndrome. The fifth also was of the Duchenne type but presented in addition a facial component such as occurs in the Landouzy-Dejerine type. The onset in each case occurred before or at about 6 years of age. Three patients were no longer ambulatory and the remaining two were markedly limited as to activity.

TABLE 1.—*Dextrose Tolerance*

Case	Fasting		30 Min.	60 Min.	90 Min.	120 Min.	150 Min.	180 Min.
1	79	25 Gm. of	369	...	135	...	56	...
2	85	dextrose	150	...	88	...	63	...
3	72	given intra-	118	85	...	56	...	66
4	59	venously	176	130	...	74	...	33

In cooperation with our metabolic unit it was proposed to determine on a quantitatively and qualitatively fixed diet:

1. The state of digestion, especially of proteins and fats, as indicated by examination of the stool.
2. The tryptic activity of the duodenal contents.
3. The daily excretion of nitrogen in the urine and its behavior with changes in the intake of nitrogen.
4. The dextrose tolerance.
5. The daily excretion of creatine and creatinine.
6. Variations in the foregoing data following therapy.
7. The clinical effect of therapy.

RESULTS AND ANALYSIS OF DATA

Stool Examinations.—In three of the five cases, stools on repeated examination were normal in gross appearance and microscopically. Muscle fibers, when present, were well digested, and fat globules could occasionally be demonstrated in a finely emulsified state with sudan III stain. In the remaining two cases the stools were unusual in the amount of grossly undigested material, which on microscopic examination, however, proved to be almost entirely vegetable in nature. There was no evidence, even in the latter cases, of disturbed digestion of meat or fat constituents of the food.

Tryptic Activity of the Duodenal Contents.—Successful intubation of the duodenum was performed in three of the five cases and determinations of tryptic activity made on the fasting contents and on the aspirations following stimulation with 20 cc. of twentieth normal hydrochloric acid.

We did not attempt to obtain prolonged secretory curves. A study of the aspirated contents of the duodenum convinced us that, unless aspiration by continuous suction of the gastric contents is maintained, dilution of the duodenal contents is sufficient to detract from the significance of a secretory curve. Therefore, normal values obtained at any period of the experiment were considered evidence of adequate secretion. Control values in normal children served as the basis for comparison.

In the second patient the fasting content showed normal tryptic activity. Specimens obtained thirty minutes and one hour later showed extremely low values.

The third patient showed normal initial values in both trypsin and lipase. Specimens one-half hour and one and one-half hours after introduction of twentieth normal hydrochloric acid gave tryptic values two and two and one-half times the initial level. Lipolytic activity maintained its fasting level.

Dextrose Tolerance.—This test was performed on four of the five patients, the intravenous method of administration of dextrose being used to obviate variations in results due to unknown factors of absorption. We used the Somogy modification of the Shaffer-Hartman method for true blood sugar. Normal limits for the fasting blood sugar level by this method are given as from 60 to 90 mg. per hundred cubic centimeters. The results are shown in table 1.

Fasting blood sugar levels of all four patients are well within normal limits. In all cases the ability to remove dextrose from the circulation does not appear to be impaired.

Excretion of Nitrogen.—Total excretion of nitrogen was determined in specimens of twenty-four hour urine collected under toluene under varying conditions of food intake. Results in one of the more advanced cases are shown in table 2 and are representative of the uniform response of the entire group.

It will be noted that the total excretion of nitrogen in the urine varies directly with the intake of protein.

On the various dietary regimens, which varied particularly as to protein and carbohydrate, each of the five patients consistently maintained a positive nitrogen balance.

Excretion of Creatine and Creatinine.—The effect of dietary variations on these urinary constituents was noted in daily specimens of twenty-four hour urine. The effect of changes in the intake of protein and of administration of large amounts of carbohydrate and insulin are noted in table 3.

From table 3 it can be seen that both creatine and, to a lesser extent, creatinine follow closely the curve of the excretion of nitrogen. Total nitrogen as in table 2 bears a direct relationship to the intake of protein. It is interesting to note that creatine and, to a lesser extent, creatinine, when expressed as percentage of total nitrogen, bear an inverse relationship to the latter. This will be discussed later.

TABLE 2.—*Excretion of Nitrogen*

Date	12/7	12/8	12/11	12/19	12/20	12/21
Food intake (Gm.)						
Protein	64	59	56	140	140	106
Fat	114	98	108	116	116	98
Carbohydrate	294	309	309	230	230	250
Total nitrogen in grams	6.32	4.99	4.78	14.12	13.86	11.66

Effect of Pancreatin Therapy on Excretion of Creatine and Creatinine.—The two patients showing some disturbance in digestion were selected for this experiment. One was treated for sixty-seven days and the other for forty-four days with a concentrated enteric coated pancreatin preparation.[11] The results in the latter patient are representative and are presented in table 4.

In neither patient did creatinuria tend to diminish with the administration of pancreatin. Its excretion was similar to that seen in table 3, in which experi-

11. Dr. David Klein of the Wilson Laboratories supplied the enteric coated pancreatin used in this study.

ment the patients received no pancreatin; i. e., it varied directly with urinary total nitrogen. Nor did the excretion of creatine compose a smaller fraction of the total creatinine.

The Effect of Therapy as Judged Clinically.—In estimating clinical results a quantitative expression of the patient's muscle power was sought. It seemed quite apparent from past experience that testimonial evidence from whatever source obtained was worthless. A series of test exercises involving the performance of definite coordinated muscle actions was therefore outlined for each patient, the ability of the patient to repeat them being noted. These quantitative figures served as an index of muscular endurance. Other test exercises were devised to determine the maximum initial performance. These records were obtained twice each week by the same trained physical therapist and were maintained for a period of nine months.

The clinical results following pancreatin therapy, administration of dextrose and insulin and of insulin alone, variations in diet from low protein to high protein and similar variations in intake of carbohydrate were evaluated on the basis of the curves obtained on tabulation of muscular performances.

When creatine and creatinine are expressed in terms of the percentage of total nitrogen excreted they bear an inverse relationship to the latter. Diminution in the intake of protein causes a fall in total excretion of nitrogen and that fraction of the latter which represents exogenous creatine and creatinine. Endogenous catabolism remaining the same, the excretion of creatine and creatinine derived from it makes up a disproportionate fraction of the total excretion of nitrogen and hence bears an inverse relationship to the latter in terms of percentage. This is most strikingly seen when the protein sparing action of large amounts of carbohydrate is involved.

For years it has been believed that there is in this disease a disturbance in glycogenesis, and on this thesis feeding of carbohydrate alone or with insulin have formed a part of the therapeutic regimen in many clinics. The striking manner in which administration of carbohydrates stops the creatinuria of starvation has been offered as corroborative evidence. In our chemical studies of the blood we cannot find support for these ideas nor have we noted any correlation of clinical improvement with periods of high ingestion of carbohydrate.

TABLE 3.—*Excretion of Creatine and Creatinine*

Date, 1933	1/5	1/6	1/9	1/15	1/29	1/30	1/31	2/1	4/4	4/5	4/6	4/7
Diet: Protein	48	47	49	48	88	100	87	86	34	49	49	39
Fat	74	74	82	74	47	61	50	48	52	52	60	42
Carbohydrate	164	171	163	169	159	151	160	160	240*	280*	278*	287*
Creatine (Gm.)	0.623	0.681	0.776	0.665	0.896	0.760	0.989	1.015	0.602	0.779	0.746	0.664
Creatinine (Gm.)	0.391	0.451	0.505	0.442	0.671	0.405	0.434	0.571	0.225	0.427	0.437	0.237
Total nitrogen (Gm.)	5.29	5.18	9.05	5.13	12.34	8.25	10.96	11.06	2.95	5.88	5.71	3.48
Creatine percentage of total nitrogen	11.7	13.1	8.5	12.9	7.3	9.2	9.0	9.1	20.4	13.2	13.0	19.1
Creatinine percentage of total nitrogen	7.3	8.7	5.5	8.6	5.4	4.9	3.9	5.1	7.6	7.2	7.6	6.8

* Values include 50 Gm. of dextrose intravenously by slow drip.

All the patients studied showed a slow progressive improvement in their ability to perform the tests outlined. However, this improvement bore no apparent relationship to the institution of various forms of therapy, including pancreatin, nor did it decline when treatment ceased. Improvement was most marked in the muscle groups most affected by the disease.

COMMENT

It appears from the results of these experiments that the patient with pseudohypertrophic muscular dystrophy does not lack the ability to digest proteins or to transform these proteins into the end products of ferment activity. There is apparently no disturbance in the formation of creatine, as one can readily note from the definite and proportionate manner in which creatinuria follows nitrogenous intake. For a long time it was felt that both creatine and creatinine had their origin solely in endogenous metabolism,[12] but our results and those of other investigators[13] indicate that there must also exist an exogenous source. The myodystrophic patient is a better subject for the study of creatine metabolism than the normal person and in excretion of creatine is analogous to the diabetic patient as regards dextrose. Added proof of the dual origin of creatine is suggested in the analysis of table 3.

From a purely clinical standpoint it has been our experience that no form of therapy available at the present time acts in a specific way to halt the progress of this disease. The patients included in this report have shown definite improvement in their ability to perform their test exercises, but this progress could not be correlated with any specific form of therapy employed. Had treatment remained constant in nature we would have felt justified in claiming a certain degree of success for it. We attribute the improvement in these patients to the prolonged period of hospitalization, which included adequate diets, and, what is perhaps more important, to the regulated daily routine and physical activity, including that involved in the performance of the test exercises. That regulated exercise is of importance was pointed out long ago and becomes apparent when one notes the harmful

TABLE 4.—*Effect of Pancreatin Therapy on Excretion of Creatine and Creatinine*

	Period 1 (Av. 3 Days) Pancreatin-Low Protein	Period 2 (Av. 3 Days) Pancreatin-High Protein	Period 3 (Av. 3 Days) Pancreatin-High Protein-Insulin 10-10-0
Protein intake (Gm.)	60	129	108
Urinary nitrogen (Gm.)	5.360	13.210	11.920
Creatine (Gm.)	0.753	1.284	1.463
Creatinine (Gm.)	0.251	0.422	0.267
Total creatinine (Gm.)	1.004	1.706	1.730
Creatinine coefficient	3.4	5.7	3.6
Creatine percentage of total creatinine	75	75	75

12. Mendel, L. G., and Rose, W. C.: Experimental Studies on Creatine and Creatinine, J. Biol. Chem. **10**: 213, 1911.
13. Beard, H. H., and Barnes, Broda O.: The Influence of Feeding Proteins, Amino Acids and Related Substances upon Creatine and Creatinine Metabolism, J. Biol. Chem. **94**: 49 (Nov.) 1931. Gibson, R. B., and Martin, Frances T.: Some Observations on Creatine Formation in a Case of Progressive Pseudohypertrophic Muscular Dystrophy, J. Biol. Chem. **49**: 319 (Dec.) 1921.

effect of restriction of activity such as follows biopsy of the gastrocnemius muscle. Such treatment, however, offers little of lasting value in the face of the seemingly inexorable inroads which this disease makes on the muscle.

What then is the path of the future? Recent work has taught us much of the physiology of muscle and has clarified some of the intricate mechanisms involved.[14] We know that creatine plays a vital part in the initiation of muscular contraction and that it occurs in loose combination with phosphorus. From a study of the chemistry of dystrophic muscles, Nevin [15] has shown that the usual breakdown of creatine-phosphoric acid does occur, differing but quantitatively from the normal. The ability to resynthesize this compound to its initial value also is retained. Differences are apparently quantitative rather than qualitative, and one is inclined to study more closely the known constituents of muscle to ascertain whether any substance is markedly deficient.

Such a deficiency has been noted clinically to exist in the coloring of the dystrophic muscle. Muscle pallor has been recently emphasized by Meldolesi.[10] This lack of adequate coloring led us to a review of the literature on muscle pigment and we found that the substance had been almost entirely forgotten in the study of the intricate processes which comprise the chemistry of muscle.

In 1887 MacMunn [16] described a number of tissue pigments, naming the one found in muscle myohematin. Gunther [17] in 1921 spoke of myoglobin and recognized that the pigment was not identical with hemoglobin. Kuhne [18] twenty years before MacMunn presented evidence to show that this muscle pigment had a respiratory function. More recently the study of this pigment has been carried on intensively and its isolation in animals has been accomplished by Theorrel [19] and later by Watson.[20]

As yet no place has been found for this substance in the economy of muscular contraction. It seems unlikely that nature has provided skeletal muscle with a substance which has tremendous oxidizing properties [21] (ten times that of hemoglobin) unless this substance plays an important role in the chemistry of muscular contraction. Eggleton [22] has shown that creatine diffuses rapidly from fatigued muscle and that this diffusion ceases when oxygen is supplied. In the lungs there is provided a delicate network of capillaries closely associated with specialized alveolar epithelium for gaseous exchange. In the muscle, where there must occur a rapid diffusion of oxygen from the capillaries, it would seem that a substance such as myoglobin would be essential. That myoglobin may indeed supply this mechanism has recently been shown by Millikan,[23] who by photoelectric spectroscopy has proved that it acts as a short-time oxygen store in the muscle to tide it over periods of oxygen want in each contraction.

We feel that when more is known of the place this pigment substance occupies in the economy of muscular processes we shall have found an important clue to the treatment of the myodystrophic patient. Quantitative and qualitative studies of the myoglobin content of muscles in various pathologic states and their correlation with known facts of the chemistry of these muscles will be necessary to evaluate the clinical importance of myoglobin. Such studies are in progress.

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17. Gunther: Arch. Path. Anat. Physiol. **230**: 146, 1921.
18. Kuhne: Arch. f. path. Anat. u. Physiol. **33**: 79, 1865.
19. Theorrel, Hugo: Biochem. Ztschr. **252**: 1 (Aug. 20) 1932; **268**: 46, 55 (Jan. 22) 1934.
20. Watson, R. H.: Biochem. J. **29**: 2114 (Sept.) 1935.
21. Annual Review of Biochemistry, 1938.
22. Eggleton, P., and Eggleton, G. P.: Biochem. J. **21**: 190, 1927.
23. Millikan, G. A.: Proc. Roy. Soc. London, s.B. **120**: 366 (June 2) 1936; **123**: 2181 (July 1) 1937.

SUMMARY AND CONCLUSIONS

1. Five patients with pseudohypertrophic muscular dystrophy were studied to determine whether a deficiency in the external secretion of the pancreas forms a part of the syndrome.

2. No evidence could be found from a study of the stools, duodenal contents and urine that the pancreas is involved.

3. Improvement while under observation was found to be unrelated to specific treatment.

4. It appears that muscle pigment or myoglobin is of importance in the economy of muscular processes.

THE TREATMENT OF CARDIAC IRREGULARITIES

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One of the most experienced cardiologists [1] has estimated that serious cardiac failure is accompanied by auricular fibrillation in more than half the cases. Experienced practitioners know that extrasystoles are at least as frequent in cases coming to a doctor's office. Therefore it becomes apparent that the treatment of the cardiac irregularities is one of the important services rendered by the physician to his clientele. Moreover, the treatment of the cardiac irregularities is today, comparatively speaking, very efficacious and easily carried out.

I shall first discuss the treatment of auricular fibrillation because this makes up nearly one half of all the cases of cardiac irregularity that one has to treat and because it has a very harmful effect on the pumping mechanism of the heart. Eyster and Swarthout [2] have shown that the mere presence of auricular fibrillation in a dog's heart reduces the output of the heart by an average of 40 per cent and reduces the blood pressure on an average of 35 per cent. Lewis [3] demonstrated that auricular fibrillation not only reduces the output of the heart but also may increase the venous pressure even in an animal with an otherwise normal heart. These experiments indicate that the appearance of auricular fibrillation in hearts with a valvular defect or with a damaged myocardium is a most serious occurrence. Every experienced physician has noted that patients with mitral stenosis often do very well for many years but that the onset of the absolutely irregular pulse, which is synonymous with auricular fibrillation, brings about cardiac failure, which from that time on is present in some degree unless the auricular fibrillation is properly treated. I have seen athletes performing creditably in competition despite the pres-

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1. Lewis, Thomas: Diseases of the Heart, New York, Macmillan Company, 1933.
2. Eyster, J. A. E., and Swarthout, Edith C.: Experimental Determination of the Influence of Abnormal Rhythms on the Mechanical Efficiency of the Heart, Arch. Int. Med. **25**: 317 (March) 1920.
3. Lewis, Thomas: Fibrillation of the Auricles: Its Effects upon the Circulation, J. Exper. Med. **16**: 395, 1912.

ence of a mitral stenosis. But as soon as auricular fibrillation began, symptoms of breathlessness and dropsy appeared and from that time on the former athlete was more or less of an invalid and could at the best carry out duties entailing only very moderate exercise.

In man, the effect of untreated auricular fibrillation is largely to increase the venous pressure and to decrease the output of blood leaving the ventricles during each minute. Through the influence of vasomotor adaptation, the tendency for blood pressure to drop is usually counteracted. The reduction in ventricular output is due largely to the rapid rate of the ventricles, to the large number of premature and abortive contractions of these chambers and to auricular paralysis. Digitalis given in sufficient amounts will reduce the ventricular rate to the optimum, and in reducing the rate of the ventricles the number of premature and abortive contractions becomes very small indeed. It is therefore by partially blocking conduction from the fibrillating auricles to the ventricles that digitalis brings about its remarkably favorable influence on the heart in auricular fibrillation.

When one sees a patient with auricular fibrillation for the first time, the ventricles are usually beating with an absolutely irregular rate of from 100 to 160 beats a minute. The exhibition of sufficient amounts of digitalis will reduce the rate of the ventricles to a value of from 60 to 70 beats a minute, which in most adults I find to be the optimal rate when auricular fibrillation is present. The effect on the patient is remarkable. As a rule, as soon as the rate is reduced to the optimal value the patient's dyspnea lessens, tenderness and enlargement of the liver recede, edema begins to become absorbed and to be excreted by the kidneys, and the cyanosis tends to diminish. The increased venous pressure, which is the main factor in causing the symptoms of dyspnea, edema and swelling of the liver, drops to normal values; measurements of circulation time and of minute volume show that the output of the heart has approached the normal, even when serious valvular defects and myocardial damage are present.

It is true that digitalis increases the mechanical efficiency of the heart muscle fibers, as Visscher [4] has shown, but when auricular fibrillation is present the reduction in the ventricular rate is at least as great a factor in bringing about compensation in cardiac failure, if not a greater one.

METHOD OF GIVING DIGITALIS

There has been a great deal of discussion as to the method of giving digitalis, and I shall spend some time in discussing this, emphasizing the methods that have proved themselves of great value in the treatment of a large number of cases at the Minneapolis General Hospital and at the University outpatient heart clinic. I shall discuss mainly the use of preparations of digitalis purpurea for preparations of this drug are now carefully standardized in terms of the cat unit.[5] This drug has now been so thoroughly studied that it is known approximately how much a patient should be given to get a desired effect and just about what the toxic dose for a given patient is. I shall mention briefly the use of preparations from digitalis lanata. In my opinion 1 cat unit (0.65 cc. of tincture or 0.065 Gm. [1 grain] of U. S. P. powdered leaf) to each 10 pounds (4.5 Kg.) of body weight when anchored in the body gives very nearly the optimal effect in lowering the ventricular rate in auricular fibrillation. It is also with but rare exceptions a perfectly safe amount. If this amount does not effect the desired lowering of the ventricular rate, a little more (from 10 to 30 per cent) most certainly will. On the other hand, not more than one patient in fifty will show signs of digitalis intoxication with this amount, and the degree of intoxication will not be serious. Stopping the administration of digitalis for from twenty-four to seventy-two hours will relieve the symptoms of intoxication and no harm will have been done. Moreover, the administration of 1 cat unit a day will on the average hold the ventricular rate of a patient weighing 150 pounds (68 Kg.) at rest and free from nervousness at the optimal point. In other words, the anchored digitalis is removed from the body at the rate of approximately a cat unit a day. Doses of digitalis of this size will not reduce the volume flow through the coronary arteries nor injure the myocardium. One cat unit a day may be given to the 150 pound patient for years without danger. If vomiting necessitates rectal administration, the same dose is to be given as for the oral administration.

Whether one uses tincture or whether one uses pills or capsules of the powdered leaf is in my opinion immaterial provided the tincture is fresh and is standardized accurately. As a rule equally good results will be obtained by the two forms of the drug.[6] If the patient is only moderately decompensated, seven days may be taken for optimal digitalization. In this case 21 cat units would be given to a patient weighing 150 pounds to be used up in seven days: 6 cat units to supply the loss of digitalis in the six days following the day on which the drug is first given and 15 cat units for the optimal amount to be anchored in the body.[7] It is well if the patient can be seen by the physician daily, but many of our dispensary patients are not seen until the week has passed. If the ventricular rate is above 70 when the patient returns and is resting quietly in the examining room and is not excited, we give 2 cat units a day until the heart rate is between 60 and 70 beats a minute. When this rate has been reached, we give 1 cat unit a day. It is best if the physician can see his patient every day or two to control the rate by giving a little more or a little less digitalis for the next four weeks, but many of our patients cannot return for one or two weeks, and it is rare not to find the pulse rate approximately the same. A little more or a little less digitalis will bring about the desired rate (60-70).

In our dispensary practice we often give the calculated optimal amount within a shorter period if the patient is badly decompensated. For example, we frequently give a patient weighing 150 pounds 17 cat units throughout a three day period, during which time a

4. Visscher, M. B.: The Energy Metabolism of the Heart in Failure, Minnesota Med. **21**: 85 (Feb.) 1938.

5. A cat unit as used in this paper is the amount of drug per kilogram of body weight necessary to kill a cat in one hour under the standard conditions of the original Hatcher-Brody method. The cat unit as determined by other methods such as the Magnus differs considerably from the Hatcher-Brody cat unit. The value of the cat unit lies in the fact that, by determining the body weight of the patient, one can calculate approximately the amount necessary to obtain the optimal digitalis effect and still be safely below the level of toxic effects of the drug. Maintenance dosage can also be expressed in cat units per day. At present digitalis is standardized according to the U. S. P. XI so that 0.65 cc. of the tincture or 0.065 Gm. (1 grain) of the powdered leaf is 1 Hatcher-Brody cat unit. In the previous editions of the U. S. Pharmacopeia 1 cc. of tincture or 0.1 Gm. of the powdered leaf contained 1 cat unit. One-tenth Gm. (1½ grains) of the standard U. S. P. XI powder is equivalent to 1.6 Hatcher-Brody cat unit.

6. The tincture should not be given in drops but the required amount should be measured out in a measuring glass. I prefer to mix 0.6 cc. of tincture of digitalis with 3.4 cc. of aromatic elixir and give this fairly pleasant mixture in this dose, each drachm (4 cc.) representing 1 cat unit.

7. Assuming that the patient has had no digitalis for at least three weeks. If the patient has had digitalis recently, 2 cat units a day is given until the pulse rate reaches 60-70.

visiting nurse counts the ventricular rate with the stethoscope during daily visits to the patient's home or to a rest home in the city if the patient is from out of town. The nurse reports late each afternoon to the physician in charge of the case.

When the patient returns on the third day, the dispensary physician gives 1 or 2 cat units a day for the next three days, depending on whether the ventricular rate is in the neighborhood of 60-70 or higher. Given in this way we have seen digitalis poisoning occur only infrequently, and we have yet to see the first case of dangerous intoxication. On the other hand, the results on the ventricular rate have nearly always been excellent.

In our hospital practice we usually attempt to get the optimal result more quickly. As a rule we give 15 cat units to the 150 pound patient within the first thirty-two hours, one third of the calculated amount being given at once and one sixth every eight hours for four doses. An attempt is made to hold the ventricular rate at the optimal point by the exhibition of 1 cat unit a day if the optimal rate has been reached at the end of from forty to forty-eight hours. If this rate has not been reached we give 2 cat units a day until the rate is between 60 and 70. After this 1 cat unit a day will usually hold the rate at this point. It may be necessary to give a little more or a little less, but if the patient is seen each day the desired amount can readily be found by observation of the pulse rate with the patient at rest and in a nonexcited state.

Occasionally we have a desperate case of heart failure with auricular fibrillation with a high ventricular rate (150-200) in which it appears desirable to reduce the rate even more rapidly. In such a case we resort to intravenous medication. In my opinion digitalis lanata preparations are best for this purpose, though one can dilute an ordinary tincture with saline solution and inject intravenously or use ampules of a well known preparation such as digalen or digifolin. Eight cat units of digitalis purpurea can be given safely at one injection to a patient weighing 150 pounds. I prefer to give 1 mg. of digilanid C [8] or 1 mg. of digoxin to such a patient. Both of these are preparations of digitalis lanata. The report of the following case will illustrate how efficiently these preparations can work:

A woman aged 56, with high blood pressure and electrocardiographic evidence of coronary arteriosclerosis, suddenly had dyspnea and orthopnea with auricular fibrillation. After sticking it out for one week at home she entered the hospital, showing 3+ edema of the lower extremities and some puffiness about the eyes. Cyanosis, ascites and venous distention of the vessels of the neck were present. The apical rate was 145 and totally arrhythmic. The venous pressure at the level of the right auricle was 17 cm. of water. There were rales at both bases as high as the angle of the scapula. The liver was down 6 cm. The vital capacity was 900 cc. She was given 1.6 mg. of digilanid C shortly after the examination on admission. Two hours later the apical rate was 84, the venous pressure 8 cm. of water and the vital capacity 1,600 cc. She was given digilanid C orally, 0.8 mg. a day, under which her pulse ranged between 60 and 80 during the following week. Twenty hours after admission all rales had disappeared, cyanosis had disappeared and the dyspnea had lessened remarkably. On the second day in the hospital the fluid intake was 600 cc. and the output 2,200 cc. During the first week in the hospital the fluid output exceeded the intake by 6,200 cc. and all visible edema had disappeared. On the fourth day the liver was back at the costal margin; on the third day the vital capacity was 2,400 cc., which was about her normal value. On the tenth day the patient was allowed up and around and showed no signs of dyspnea, nor had she any distress. No other treatment other than rest and digitalis was used.

This case illustrates not only how digitalis properly given can favorably affect auricular fibrillation complicating cardiac failure but how rapidly a digitalis preparation can accomplish the result when intravenously administered.

It cannot be denied that there are a few exceptions to the foregoing rules for administration of digitalis; occasionally digitalis seems to have no appreciable effect on conduction of the impulse from the auricles to the ventricles and therefore does not slow the ventricular rate, and a small percentage of patients show toxic symptoms before the optimal results in reducing ventricular rate can be accomplished. Not a few patients will need more than 1 cat unit to 10 pounds of body weight anchored in the body in order to produce optimal slowing of the pulse rate. Usually not more than from a 10 to 30 per cent increase is necessary to accomplish this. A very few patients will need less than the calculated optimal dose. This condition is usually found in coronary disease or in other conditions that in themselves reduce conductivity through the bundle of His. These cases often show apical rates of 100 or less before any digitalis has been given. When the apical rate is less than 110 it is well to use smaller amounts of digitalis than that previously recommended because conductivity from auricles to ventricles may already be impaired. If the rate is around 80 only 2 cat units a day should be given and the pulse should be watched from day to day until the physician is certain that the rate is not going to fall below 60. In hyperthyroidism digitalis usually fails to lower ventricular rate and its value is questionable. The administration of compound solution of iodine will usually reduce the rate somewhat. Operation should be carried out when it is thought safe, and after operation the fibrillation will disappear in more than 50 per cent of the cases. In toxic conditions associated with fever the dosage should be definitely smaller.[9] The effect will often leave much to be desired, but according to the present state of our knowledge it seems unwise to go beyond one-half the usual dose in fevers with toxemia.

There are patients who are sensitive to digitalis and the reduction of their ventricular rate may be difficult. It is necessary to proceed with smaller doses, and it may be impossible to get the rate below 80-90. When more digitalis is given nausea, vomiting or extrasystoles may appear, and the patient who was beginning to compensate moderately may now show signs of decreasing compensation. One should give as much digitalis as the patient can stand without showing signs of nausea, vomiting or extrasystoles. Coupled beats developing during the course of digitalis treatment mean severe digitalis intoxication, and the drug must be withheld until all extrasystoles disappear. It may then be cautiously given again.

The ventricular rate should never be allowed to drop below 60. Lowering the pulse rate below 60 does not increase but rather decreases the efficiency of the cardiac

8. This is a preparation of digitalis lanata studied by Dr. M. B. Visscher pharmacologically and now being investigated clinically in the Minneapolis General Hospital. The drug, prepared by the Sandoz Company, has not yet been released to the profession.

9. Edmunds, C. W.; Smith, R. G., and Moyer, C. A.: The Sensitivity of the Diphtheritic Heart to Digitalis, J. Pharmacol. & Exper. Therap. **61**: 286 (Nov.) 1937. Hirschfelder, A.; Rieck, J.; Kucera, F. J.: The Effect of High Temperature on the Action and Toxicity of Digitalis, ibid. **15**: 427 (July) 1920.

pump. Signs of decompensation usually do not reappear until the rate falls to 50 or below, but 60 should be the lower limit of the pulse rate at rest.

QUINIDINE

Up to this point I have been discussing the treatment of auricular fibrillation in patients who had in addition a valvular disease or a diseased myocardium. There are a few patients who have attacks of auricular fibrillation unassociated with any discoverable organic heart disease. These attacks may be associated with great excitement or emotion. For example I have seen one patient who had a number of attacks of auricular fibrillation following the excitement of the sexual act. Occasionally severe physical exertion will bring on an attack. I have observed one such case in a track athlete. Attacks of auricular fibrillation may follow infectious diseases such as influenza and pneumonia. Drugs and chemicals may induce attacks. In my experience attacks of auricular fibrillation following drinking bouts are not at all uncommon. The outlook in these cases is excellent as a rule and the patient usually suffers only from palpitation, smothering, weakness, mild precordial distress or a little dizziness. Occasionally cardiac failure will develop even though there is no evidence of the presence of organic heart disease. As a rule the fibrillation is easily terminated in these cases and normal rhythm restored by the use of quinidine. As far as my reading goes all who write on this subject agree that quinidine is the drug of choice in auricular fibrillation unaccompanied by serious organic heart disease.

On the other hand there are many competent cardiologists who warn against the use of quinidine to terminate auricular fibrillation in cases of organic heart disease or who overemphasize the dangers of quinidine in the treatment of auricular fibrillation complicated by organic disease of the heart. We have used quinidine to terminate auricular fibrillation for the past seventeen years and during this period my associates and I at the Minneapolis General Hospital and at the University Heart Clinic have treated with quinidine more than 500 patients having auricular fibrillation. In approximately 65 per cent of these cases the auricular fibrillation has been stopped and the ventricular rhythm has become regular. Moreover we have prevented the return of fibrillation in nearly every patient who has continued the daily dose prescribed for prophylaxis. In general we are well satisfied with the results of quinidine therapy in our cases. Many patients who were uncomfortable and unable to carry out even moderate physical exertion on digitalis therapy alone were made easy and recovered considerable ability to carry on physical exertion after quinidine had restored normal rhythm.

That there are grave dangers inherent in the use of quinidine I do not deny. Quinidine is a drug which is toxic for the heart muscle. It reduces the strength of contraction of the heart muscle and in our early use of the drug we occasionally brought on cardiac failure while attempting to terminate auricular fibrillation.[10] Since then we have learned that the use of quinidine in treating auricular fibrillation in hearts that have been decompensated or that present serious organic disease must be preceded by thorough digitalization of the heart. Under these circumstances cardiac failure will not develop even when large doses of quinidine are given. Before giving quinidine we give sufficient digitalis to bring the ventricular rate to values around 60-70. This rate is maintained by daily doses for approximately two weeks before quinidine therapy is started. If the patient was severely decompensated before digitalis therapy was started we might wait a little longer before beginning the quinidine therapy. Under these circumstances we do not fear the adverse effect of quinidine on the mechanical efficiency of the heart muscle.

Another danger that is only rarely encountered when quinidine is used is that of asystole. I myself have observed only one case:

> A woman aged 36 who had rheumatic fever in her youth was seen by a local physician in an advanced stage of cardiac failure associated with mitral stenosis and auricular fibrillation and a greatly dilated heart. She was overdigitalized and during the period that her heart was showing coupled beats she was given quinidine. When 30 grains (2 Gm.) was given unconsciousness developed. Her physician observed five attacks of asystole in three hours and called me in consultation. She recovered and her heart was kept regular for three years. Auricular fibrillation reappeared and in a few months she died of multiple embolism.

It should be noted that these emboli did not develop during the period when quinidine restored and maintained regular rhythm but at a time when the auricles were fibrillating. In reviewing this case critically I would say that two mistakes were probably made. Quinidine should not be given in doses larger than 15 grains (1 Gm.) a day when there is evidence of digitalis poisoning because there may result therefrom a dangerous summation of the toxic effects of both drugs. This patient was suffering from digitalis intoxication (coupled beats) when the quinidine was administered. It would have been better to wait one week after all signs of toxicity had disappeared before starting quinidine. Moreover, this patient had a markedly dilated heart as shown by x-ray and postmortem examination. In such cases it is advisable either to withhold quinidine or to proceed more slowly in increasing the dose.

Embolism is a danger that undoubtedly is associated with the use of quinidine but one that has been overemphasized in my opinion. The paralyzed auricle is a favorite site of mural thrombi. When the auricles beat again a piece of thrombus may be dislodged and become an embolus. In my experience embolism is less frequent following the restoration of regular rhythm with quinidine than it is in cases in which only digitalis is used and in which the auricles are allowed to fibrillate. Viko, Marvin and White[11] have shown that embolism occurred in 4.5 per cent of their untreated cases and in 3.1 per cent of their cases treated with quinidine. Korns[12] questions the greater incidence of embolism in quinidine-treated cases. Parkinson and Campbell,[13] after a careful analysis of embolism in quinidine therapy, came to the conclusion that this danger has been overemphasized. I have not infrequently seen embolism follow resumption of fibrillation in auricles that had been kept regular for long periods on quinidine.

Cases of syncope occur rarely. I myself know of only one such case. The patient was treating himself and it was proved that he had been taking excessive doses at times. Epileptiform convulsions are also rare

10. Eyster, J. A. E., and Fahr, George: Observations on the Use of Quinidine in Auricular Fibrillation, Arch. Int. Med. **29**: 59 (Jan.) 1922.

11. Viko, L. E.; Marvin, H. M., and White, P. D.: A Clinical Report on Quinidine Sulfate, Arch. Int. Med. **31**: 345 (March) 1923.

12. Korns, H. M.: An Experimental and Clinical Study of Quinidine, Arch. Int. Med. **31**: 36 (Jan.) 1923.

13. Parkinson, J., and Campbell, M.: Quinidine Treatment of Auricular Fibrillation, Quart. J. Med. **22**: 281 (Jan.) 1929.

episodes in patients who are abnormally sensitive to quinidine. I have observed one such case in the University Hospital. Convulsions followed a dose of only 6 grains (0.4 Gm.). The most common manifestations of sensitivity to quinidine are epigastric distress, nausea, vomiting, headache, diarrhea, ringing in the ears, palpitation and apprehension. These symptoms should lead to a lowering of the dosage and to a less rapid increase in dosage up to the point at which auricular fibrillation is stopped. Very frequently one will be successful with a less rapid increase in dosage. If these symptoms do not disappear and if they become annoying it is best to stop the quinidine altogether.

Having first stated the disadvantages of quinidine, I shall now give an account of its value in treatment. There is no question in any one's mind that quinidine is the treatment *par excellence* in auricular fibrillation not associated with serious organic heart disease and when auricular fibrillation in hyperthyroidism is still present two weeks after thyroidectomy. As a rule these cases show regular heart rate on small doses of quinidine and unpleasant episodes are very rare. Kerkhof [14] and others have shown that the efficiency of the heart is increased 25 per cent in mitral stenosis with auricular fibrillation when regular beating of the auricles is restored even though the heart was kept at an optimal rate by the use of digitalis during the period of fibrillation. I therefore recommend a trial of quinidine in all cases of mitral stenosis with auricular fibrillation in which the total transverse diameter of the heart is not enlarged more than 20 per cent and when the abnormal rhythm has not been present for more than six months. The physician who is experienced in the use of quinidine may extend these limits, but the beginner should stay within them. The use of quinidine must be preceded by digitalization and the heart must have been well compensated for two weeks before the quinidine therapy has been started. Digitalis must be given through the treatment with quinidine; we often continue it after the cardiac rate has become regular in cases of marked cardiac enlargement. Quinidine must be given every day after the rhythm has become regular because most hearts will revert to the absolutely irregular rate from weeks to months after the drug has been discontinued. Patients must be warned not to discontinue the drug. The average case will continue with regular rhythm on 9 grains (0.6 Gm.) a day. Occasionally we give 12 grains (0.8 Gm.) a day. Rarely we give 1 Gm. or 15 grains, a day to keep a heart regular. I have given doses of 9 and even 12 grains a day for as long as ten years and have never yet had occasion to regret it. I believe that continuance of regular rhythm in mitral stenosis will increase life expectancy materially.

Physiologists agree that the auricles contribute to the filling of the ventricles. Wiggers [15] states that they contribute on an average 35 per cent of the total filling, which would indicate that the auricle is an important part of the pump mechanism. If the auricles do not contract, venous pressure must rise or the cardiac output will fall even in a normal heart. Rise in venous pressure is the fundamental mechanism in bringing out the symptoms of dyspnea and edema. For this reason, and also because many patients feel much better when the heart rate is regular, we try quinidine therapy in cases of auricular fibrillation associated with hypertensive heart disease and coronary arteriosclerosis. In these older patients quinidine seems to have no more contraindications than in the younger ones with mitral stenosis. The same rules for administration apply in these cases.

We administer quinidine in 3 grain (0.2 Gm.) tablets. One tablet is given on the first day to test the patient for intolerance to the drug. The next morning one tablet is given at 8 o'clock and another at 9. On the third day one tablet is given at 8, one at 9 and one at 10 a. m. The dosage is increased one tablet a day, all the tablets being given at 8, 9 and 10 a. m. It might even be safer to use 2 grain (0.13 Gm.) tablets and proceed in the same way but more slowly. We prescribe as high as twelve tablets, or 36 grains (2.3 Gm.), a day but I would recommend that the inexperienced physician stop at a daily dose of 24 grains (1.5 Gm.). With this dose at least 50 per cent of all cases should have regular rhythm restored. The physician should prescribe 9 grains (0.6 Gm.) a day for the purpose of maintaining the regular rhythm as long as possible. If a patient weighing 150 pounds was severely decompensated before starting the digitalis I recommend continuing with 1 cat unit a day in addition to the 9 grains of quinidine. During the treatment the patient should be in a hospital or at home with a nurse to observe the pulse and general condition until the pulse becomes regular. Many of our patients are treated at home. A visiting nurse sees the patient once a day and reports to me each evening until the pulse is regular.

The incidence of auricular flutter is much less than that of fibrillation. In this condition the auricle is beating at a rate of from 260 to 320 a minute, but as a rule there is a 2:1 heart block. In my experience auricular flutter is frequently found in hearts that present only a moderate degree of organic disease, and the patients when seen by the physician are not suffering from the severest degrees of cardiac failure despite the fact that the ventricular rate is between 130 and 160 beats a minute. Occasionally one sees a case of auricular flutter in which there is no heart block; then the ventricle is beating at a rate of 260 or over. This is a most dangerous rate and even in an otherwise normal heart cannot go on unchecked if the patient is to live. The rate of the ventricle must be reduced at once, and with very rare exceptions this can be easily brought about by the exhibition of digitalis. In the case of the very high ventricular rates in which no block is present I recommend strongly the intravenous use of a preparation of digitalis, preferably a lanata preparation, because of the rapidity with which they work when given intravenously. When a 2:1 heart block is present and the patient is not suffering critically, digitalis may be given orally or rectally in such doses that the optimal amount of 1 cat unit to 10 pounds of body weight is introduced into the body within a period of from twenty-four to thirty hours. This will usually increase the block to a 3:1 or 4:1 block. I prefer to give enough digitalis to keep the block 4:1. Very frequently the previously regular beat of the 2:1 block will become somewhat irregular after the exhibition of large doses of digtalis because the heart will slip from 4:1 block back to 3:1 block and then again into 4:1 block. A good rule is to keep the rate of the ventricle between 60 and 70 beats a minute. A main-

14. Kerkhof, A. C.: Minute Volume Determinations in Mitral Stenosis, Am. Heart J. **11**: 206 (Feb.) 1936.
15. Wiggers, C. J.: Modern Aspects of Circulation in Health and Disease, ed. 2, Philadelphia, Lea & Febiger, 1923, p. 96.

tenance dose of 1 cat unit or more a day should be given to the patient in order to hold this rate.

In about 90 per cent of cases the auricular flutter will change to auricular fibrillation if this state of digitalization is kept up for a week or two. Digitalis is then stopped and in about 60 per cent of the cases that have gone over to fibrillation normal rhythm returns. I have found it advisable to give quinidine in those cases in which fibrillation does not develop after digitalization and in those in which fibrillation is not followed by normal rhythm after digitalis has been removed. We give quinidine to patients with flutter according to the same rules outlined for giving quinidine to a patient with auricular fibrillation. The percentage of success in bringing about return of a normal cardiac mechanism with quinidine is no greater in flutter than in fibrillation. A certain number of patients will remain refractory, and it is necessary to continue these patients on digitalis therapy in order to block conduction from auricles to ventricles. Starr [16] states that acetyl-β-methylcholine will occasionally convert auricular flutter to regular mechanism if from 30 to 50 mg. is given subcutaneously. This drug, the action of which will be discussed under paroxysmal tachycardia, can be tried for flutter when other methods fail.

EXTRASYSTOLES

Extrasystoles or premature beats are seen in the doctor's office as frequently as auricular fibrillation. Most of these cases do not present serious organic heart disease, and unless the extrasystoles occur more frequently than 12 a minute they do not affect the efficiency of the heart adversely. Extrasystoles not associated with organic heart disease are usually found in nervous, worried or apprehensive persons. I have occasionally seen an athlete retired from the squad for this irregularity. On reassurance and treatment he has soon gone back to successful competition. Frequently extrasystoles are associated with flatulence, the relief of which causes the premature beats to disappear. The patient usually does not suffer from symptoms of cardiac failure but is embarrassed and frightened by what he terms his heart "flopping" or "skipping a beat" or "stopping" for an instant or "palpitation" or a "funny feeling in the heart." Treatment in these cases requires first of all reassurance that the condition is not serious. Worry and undue fatigue must be removed. A change of environment is often useful. Sedatives such as bromides, barbiturates or codeine may be necessary to reduce excitability. Occasionally tobacco or coffee must be prohibited. Sometimes lying on the left side will evacuate gas from the stomach and get rid of extrasystoles. When these measures fail, quinidine either alone or with strychnine one-thirtieth grain (0.002 Gm.) three times a day will frequently abolish this irregularity. The quinidine is to be given in doses of 3 grains three times a day increasing to four times a day or even to 4 grains three times a day.

Extrasystoles are found in at least 10 per cent of all cases of coronary thrombosis. Masters [17] found them in 25 per cent of the Mount Sinai Hospital cases. Here they are of grave significance and quinidine must be given to prevent the appearance of ventricular tachycardia, the drug being given in doses of 3 grains every two to three hours for three or four doses. If the extrasystoles disappear the drug may be repeated every six to eight hours to prevent recurrence. Digitalis predisposes to the formation of extrasystoles and ventricular tachycardia in coronary thrombosis and should not be administered unless auricular fibrillation or flutter with ventricular rate above 95 or moderately severe cardiac failure is present. When extrasystoles occur in the course of valvular disease, in the course of hypertension or in the course of coronary arteriosclerosis they may be of serious significance, especially if they occur at frequent intervals. Quinidine or quinidine and strychnine should be used to stop them, given as already outlined. As a rule, digitalis should not be given under these circumstances.

PAROXYSMAL TACHYCARDIA

Paroxysmal tachycardia is, after all, only a very rapid and regular series of extrasystoles, starting suddenly and ending just as suddenly. I shall first discuss the treatment of paroxysmal tachycardia of auricular and junctional origin. In some cases these attacks come on infrequently and last only a short time, and in these there is no need for treatment. If the attacks come on at frequent intervals and embarrass the patient, digitalis in my experience will often prevent them. I would recommend giving as much digitalis as was recommended for treating auricular fibrillation, attempting to get the optimal amount into the body within three days and holding on 1 cat unit a day from then on. I have had more success in preventing auricular and junctional paroxysmal tachycardia with digitalis than with quinidine. On the other hand, some cardiologists use quinidine for this purpose. In my hands it has been effective only occasionally.

An attack of paroxysmal tachycardia usually leads to much discomfort and may have serious consequences in a patient who has serious cardiac disease. It is therefore necessary to know how to treat the attack. The patient is usually recumbent when the physician arrives. An ice bag over the precordium helps psychically. I would first try pressing on the carotid sinus, as this occasionally stops an attack. One places the second and third fingers over the carotid artery at the level of the thyroid cartilage and presses the artery very firmly back against the transverse processes of the cervical vertebrae. It should be tried first on the right carotid and then on the left. If this doesn't stop the attack I try pressing on the eyeballs. Sometimes the patient can stop an attack by closing the glottis after a deep inspiration and then pressing hard. A feather, tongue depressor or other object pressed or rubbed against the posterior pharynx so as to cause vomiting will also occasionally stop an attack. Weiss and Sprague [18] recommend giving from 1 to 2 drachms (3.8 to 7.5 cc.) of fresh syrup of ipecac to cause nausea and vomiting. If the effect is not obtained after forty-five minutes the dose is repeated or increased a little. This method is very efficacious. Acetyl-β-methylcholine has recently been recommended [16] for the treatment of paroxysmal tachycardia of auricular or junctional origin. It is probably the surest in its action of all the drugs recommended for treating attacks. There seems to be no great danger connected with its use. I have seen one case in which there was

16. Starr, Isaac, Jr.: Further Studies on Paroxysmal Tachycardia, Am. J. M. Sc. **191**: 210 (Feb.) 1936.

17. Masters, A. M.; Dack, S., and Jaffe, H. L.: Disturbances of Rate and Rhythm in Acute Coronary Artery Thrombosis, Ann. Int. Med. **11**: 735 (Nov.) 1937.

18. Weiss, Soma, and Sprague, H. B.: Vagal Reflex Irritability and the Treatment of Paroxysmal Tachycardia with Ipecac, Am. J. M. Sc. **194**: 53 (July) 1937.

a short period of unconsciousness following a dose which was about double the amount I recommend in this paper. The drug is a powerful stimulator of the vagus and should not be used when there is a tendency to asthma, as its injection will bring on an attack. It produces sweating, vomiting and vasodilatation and occasionally substernal pain and defecation. I would recommend trying 20 mg. of the drug in younger patients and 30 in older patients. The drug is obtained from Merck & Co. in powder form and must be dissolved in water and prepared for hypodermic use. It is very soluble and 50 mg. can be given in 1 cc. The drug is given subcutaneously and the deposit is massaged to increase the effect if necessary. I have not yet needed to supplement the drug effect with carotid sinus pressure, though Starr claims that 20 per cent of his patients needed it. The patient should be lying down, since he may faint if he is sitting up. If the attack does not stop in two or three minutes the dose is repeated. Correspondingly smaller doses should be used in children or very small adults. Large intravenous doses of digitalis will also stop attacks. Ten cc. of digifolin or digalen in ampules may be given to the patient weighing 150 pounds in one or two doses.

Paroxysmal tachycardia of ventricular origin, or ventricular tachycardia as it is usually designated, is not infrequently discovered in patients who seem to have no organic heart disease or cardiac enlargement. Because of the rapid rate (160-220) one often finds signs of failure even when there is no evidence of any other cardiac disease. I have a number of patients who come in at long intervals with attacks and moderately severe cardiac failure. When the tachycardia is stopped they return to a life of moderately strenuous activity. There are no signs of any cardiac failure as long as they take 9 grains (0.6 Gm.) of quinidine a day. They then become convinced that they will never have another attack, omit the drug and sooner or later return with tachycardia and symptoms. In one case which I saw in consultation with Dr. Scherer, it was necessary to give 85 grains (5.5 Gm.) in five hours in order to stop the tachycardia and relieve the alarming symptoms of cardiac failure which had developed in an otherwise normal heart. This patient was like many whom I have seen in that she had been having attacks for years, the attacks becoming progressively more severe, lasting longer and being associated with alarming symptoms of cardiac failure soon after she went off her daily prophylactic dose of 9 grains.

As a rule this type of tachycardia is found most frequently in patients with coronary disease and may then be a most serious factor. It is not at all infrequent in coronary thrombosis and in that case is the next step before ventricular fibrillation and death. The need for an efficacious drug is imperative and it is fortunate that quinidine is available. I have never failed to stop ventricular tachycardia with quinidine. In ventricular tachycardia it is well to give 3 grains of quinidine to test out the patient for idiosyncrasy to the drug and then give 6 grains an hour later. If the tachycardia has not stopped by the end of the hour, 6 grains may again be given. Even though the tachycardia may not have ceased at this time I would stop giving the drug and wait four hours before repeating it. It has been shown by Lewis [19] that the maximal effect on ventricular rate comes four hours after quinidine is given by mouth and most attacks of ventricular tachycardia will stop with a total of 15 grains 1 Gm.) given in this way. There is usually time enough to save the patient's life after the four hours has elapsed. I have had success with smaller doses and I have also had patients who needed much more. There is one question that will arise in the minds of readers of this paper, namely as to the use of digitalis in these cases. Digitalis increases the tendency to ventricular tachycardia in coronary thrombosis and, once the tachycardia is established, it probably increases the tendency to ventricular fibrillation. Therefore digitalis should not be given when ventricular tachycardia is present.

19. Lewis, Thomas: Value of Quinidine in Cases of Auricular Fibrillation, Am. J. M. Sc. **163**: 781 (June) 1922.

HEART BLOCK

The treatment of heart block in my experience is the least satisfactory treatment of any of the arrhythmias. Occasionally atropine in doses of 1/100 grain (0.0006 Gm.) will so far reduce the block in the bundle of His in cases of partial heart block that digitalis may be used safely in moderate dosage to increase the mechanical efficiency of the heart muscle. In total heart block digitalis may be given to increase the mechanical efficiency of the heart muscle without fear of any reduction in ventricular rate. When attacks of asystole with syncope are occurring, from 5 to 10 minims (0.32 to 0.65 cc.) of epinephrine subcutaneously given with massage of the area will prevent asystole and syncope for from one to two hours. At the time of asystole there is no blood flow, and if the asystole with syncope and convulsions lasts from thirty to sixty seconds epinephrine from 3 to 5 minims (0.2 to 0.3 cc.) must be given intracardially in the fourth left interspace just lateral to the sternal border. Ephedrine hydrochloride in capsules containing three-fourths grain (0.048 Gm.) may be given from four to six times a day to patients having daily attacks of Adams-Stokes syndrome due to asystole of the ventricles. These patients in my experience seem very tolerant to ephedrine and can be given large doses without very unpleasant side effects. I have apparently inhibited the Stokes-Adams syndrome for long periods by chronic doses of ephedrine, although it must be admitted that it fails in some cases to prevent attacks. Wherever possible an electrocardiogram should be taken because the Adams-Stokes syndrome may be due to runs of ventricular fibrillation or of frustrate extrasystoles. In this case neither epinephrine nor ephedrine should be given, for it only increases this tendency, but rather quinidine in sufficient doses to stop the runs of ventricular fibrillation or to inhibit the frustrate extrasystoles.

ABSTRACT OF DISCUSSION

DR. WILLIAM J. KERR, San Francisco: In the main, I agree with what Dr. Fahr has said about the treatment of disturbances in the mechanisms controlling the heart. I agree with what he said about digitalis, with one possible exception. I believe there are patients who have advanced mitral stenosis with a buttonhole mitral valve who will not do well if the ventricular rate is reduced to the level which he suggests. Some of these patients, I am sure, will be better off at a rate of from 80 to 90 than at the lower figure. Dr. Fahr wisely suggests that there is no need for the extremely rapid digitalization of patients which was suggested a few years ago. If the result can be achieved in three or four days in the average person, that is the most satisfactory method. I agree with Dr. Fahr that the dangers of quinidine have been overrated, excepting in older persons who already have some degree of heart block, to whom

I think it should be given with great caution. I believe it is far better to give the quinidine regularly about every five or six hours around the clock in preference to single doses given early in the morning. I think that if cases are chosen properly and it is given regularly throughout the day and night the results will be much higher than 50 per cent and will approach 80 per cent in practice. Dr. Fahr did not have a chance to speak of extrasystoles, paroxysmal tachycardia, ventricular tachycardia and heart block. I should like to make one point about ventricular tachycardia which I hope he will discuss in closing. It is suggested that quinidine should be used more frequently in ventricular tachycardia. If all patients with ventricular tachycardia are given quinidine there will be real trouble because a high percentage of these patients have serious vascular disease of the heart. A good many of them have block in the conduction system and since quinidine acts on the conduction system tending to increase the block as well as on the muscle, I think the dangers of making the patient worse and producing a ventricular fibrillation are considerable in this group. While there are some reports of good results in this abnormal mechanism, I believe it is a dangerous drug to use in a routine manner under these circumstances.

DR. HORACE M. KORNS, Iowa City: I wish to supplement Dr. Fahr's excellent presentation with a few remarks on the treatment of supraventricular paroxysmal tachycardia. The number of attacks may be greatly reduced by the continuous administration of quinidine sulfate in doses of from 3 to 18 grains (0.2 to 1.16 Gm.) a day. Individual attacks can be terminated by pressure over one or both carotid sinuses, pressure on the eyeballs, swallowing ice water, performing Valsalva's experiment or inducing vomiting by means of ipecac or tickling the pharynx. Attacks which are resistant to these measures may be terminated by acetyl-beta-methylcholine (mecholyl). The dose is proportional to age and body weight. From 10 to 20 mg. may suffice for patients between 10 and 20 years of age, and from 40 to 50 mg. may be required for those over 50 years of age. Sixty mg. might be needed for an obese person. The average dose is 30 mg. The drug is given subcutaneously or intramuscularly, never intravenously. If the attack does not stop promptly, pressure is applied first to one, then to the other, carotid sinus. The injection may be repeated and the dose increased within ten minutes, so that if necessary as much as 100 mg. may be given in less than an hour. If the dose is too large the heart may stop beating for as long as from thirty to forty-five seconds. Before giving mecholyl it is advisable to have ready a syringe containing one-fiftieth grain (0.0013 Gm.) of atropine, which is an instantaneously effective antidote, but beating will probably be resumed whether atropine is given or not, for it is impossible to keep the mammalian heart inhibited by vagus stimulation. If atropine is used it should be given intravenously. Quinidine is antagonistic to mecholyl, and if the patient has taken any quinidine within twenty-four hours of the time when mecholyl is given the latter may fail even if the dose employed is larger than it would ordinarily be. It has been the experience of most observers that mecholyl will stop paroxysmal supraventricular tachycardia in from 80 to 90 per cent of the cases, especially when it is used in conjunction with carotid sinus pressure. The danger is practically negligible, provided cases of asthma, angina pectoris and far advanced myocardial disease are excluded. The introduction of mecholyl means that at last a brilliantly successful remedy has been found for what is often an extremely intractable and serious disorder of the heart beat.

DR. S. A. WEISMAN, Minneapolis: I might add a few words about the treatment of auricular fibrillations with quinidine. As Dr. Fahr stated, it is important first to digitalize the patient and get the heart rate down to between 80 and 70. It is perhaps wise to cut down the digitalis to a maintenance dose before the quinidine is begun. I prefer to use a smaller beginning dose than Dr. Fahr does, because I believe that with this smaller dose the patient is more apt to establish a tolerance for the drug and not experience the toxic symptoms one so often reads about. I begin usually with 0.1 Gm. the first day, 0.2 Gm. the second, 0.3 Gm. the third and 0.4 Gm. the fourth day, given in doses of 0.1 Gm. each, one hour apart. Then begin, say, the fifth or sixth day with 0.2 Gm. every hour for three doses. The next day give 0.2 Gm. for four doses, making a total of 0.8 Gm. daily. From this point I usually give 5 grains (0.3 Gm.) every hour for three doses, then in a few days give 5 grains every hour for four doses, then after a few more days 5 grains in the first dose, then 10 grains (0.65 Gm.) in the second and 10 grains in the third. The final dose I use is 10 grains every hour for three doses. I usually quit at about 30 grains (2 Gm.) a day if the heart has not returned to normal rhythm, to which some 70 per cent have usually returned by that time. After the normal rhythm is once established, I begin to cut down the doses by 5 grains every two or three days until a maintenance dose is established. Then I continue giving, say, 10 grains or, in some cases, 5 grains, a day for years but always keep the patient on a maintenance dose of digitalis together with a maintenance dose of quinidine. The mitral stenosis group seems to be the most difficult to restore to regular rhythm. These cases are the most difficult to maintain regularity and are also the ones that are most apt to return to arrhythmia. The hypertension and coronary sclerosis groups react much more favorably to this treatment.

DR. WILLIAM DRESSLER, Berkeley Calif.: I should like to mention a remedy which I have used in Vienna, Austria, for paroxysmal tachycardia. It is magnesium sulfate, which I use intravenously in doses of 15 cc. in 20 per cent solution, and I have had in many cases an excellent result. The effect appears in about five minutes, sometimes a little sooner. The injection is performed rather quickly, particularly in ventricular paroxysmal tachycardia after coronary occlusion. It has proved very successful, in some cases really life saving. I have never seen any unfavorable effect.

DR. GEORGE E. FAHR, Minneapolis: Those who have discussed my paper have helped greatly in attempting to cover the treatment of cardiac irregularities in fifteen minutes. Dr. Kerr has stated that when he has one of those narrow buttonhole mitral stenoses it is better to hold the rate around 80-90 rather than around 60-70. I agree if he means patients with markedly dilated heart who have been decompensated for a long time and who show ventricular extrasystoles or coupled beats when the slowing of the heart gets down below 80-90 beats per second. Signs of digitalis intoxication are always indications for less digitalis. I am surprised that Dr. Kerr can get normal rhythm with the use of quinidine in 80 per cent of his fibrillators. I have never been able to get more than 65 per cent. In cases of arteriosclerotic heart disease I am able to get a percentage up around 80 but in mitral stenosis I have great difficulty in getting more than 65 per cent to become regular. It is possible that Dr. Kerr's method of administering quinidine is better than mine. I shall try it. I am surprised about what Dr. Kerr said as to the use of quinidine in ventricular tachycardia. I have always used it in treating cases of ventricular tachycardia. In my opinion it is especially indicated when ventricular tachycardia follows a coronary thrombosis. Ventricular tachycardia is the next step on the way to ventricular fibrillation. I believe it is necessary to give quinidine to stop the ventricular tachycardia and prevent ventricular fibrillation. I have given as high as 85 grains (5.5 Gm.) of quinidine in a twenty-four hour period because I believe it is absolutely necessary to stop the tachycardia. I am grateful to Dr. Korns for discussing the use of acetyl-beta-methyl choline, or mecholyl, in the treatment of paroxysmal tachycardia of supraventricular origin. As far as my experience goes I have been 100 per cent successful in stopping paroxysmal tachycardia of supraventricular origin with this drug. I believe Dr. Weisman's method of starting off with smaller doses and increasing the amount of quinidine more slowly is probably safer than my own. Dr. Weisman carries out the treatment of auricular fibrillation by his method in the ambulatory cases in his private practice in Minneapolis. He has told me that he has never had to regret the use of quinidine in that practice. I would disagree with one thing in his method: when he gets up to a fairly large daily dose, he then proceeds as fast as I do. That would be the point at which I would go more slowly. Dr. Dressler has suggested a new remedial agent for the treatment of paroxysmal ventricular tachycardia and I shall be delighted to try it out. No one need fear the use of intravenous magnesium sulfate if there is a hypodermic of calcium chloride handy on the tray in case there is trouble with the respiratory center.

PATHOLOGY OF THE PLACENTA

WITH SPECIAL REFERENCE TO INFARCTS AND THEIR RELATION TO TOXEMIA OF PREGNANCY

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The pathology of the placenta may be better understood and appreciated if approached from the standpoint of the life cycle of this organ and the influences to which it is subjected from the time of implantation to full term. Accordingly, certain fundamental basic facts will be considered and the pathologic changes which may arise from each of these will be discussed.

Since this article deals particularly with placental infarction, no attempt will be made to consider in more than a brief way the various other pathologic conditions, which are fully discussed in the textbooks and literature.

Embryologically, the anlage of the placenta is trophoblastic tissue, one of the primary germ layers. As such it is endowed with peculiar invasive qualities by virtue of its proteolytic enzymes, whereby it is able to attach itself to the uterine decidua, embed in it, open maternal blood vessels and create for itself a vascular bed. Potentially therefore one would expect an aberrant growth of such tissue, especially in the period of its greatest activity, the early months of pregnancy, to be highly malignant and destructive.

Chorio-epithelioma may thus arise if trophoblastic tissue takes on a malignant change. Marchand demonstrated the origin to be in the syncytium and Langhans layer of the villi. The growth may simulate villous structure, or it may be quite atypical in arrangement of the cells. While it may develop in association with early normal pregnancy or abortion, it is particularly liable to appear in association with or following hydatidiform mole. In many cases there is an interval of months or even years between the pregnancy and the appearance of the growth.

On account of the destructive and vascular character of the growth, uterine hemorrhage is an early symptom. Metastases occur through the venous channels and appear particularly in the vagina, vulva and lungs. X-ray examination of the chest may reveal pulmonary metastases. The Aschheim-Zondek test shows an unusually high concentration of the hormone and is of great value in diagnosis and prognosis. Unfortunately the clinical course of the growth is more conclusive proof of its malignant tendency than the microscopic examination, as spontaneous disappearance of the growth has been observed.

Accompanying the penetration of trophoblastic buds into the uterine decidua at a very early stage, vascularization of the future villi is effected through further differentiation of the trophoblastic layer, until the future placental area develops a rich circulation. Potentially therefore, in a tissue which is so highly vascularized, excessive capillary growth may occur, even to the extent of tumor formation. In this manner angioma of the placenta may arise.

In sectioning fixed placentas in strips from 0.5 to 1 cm. thick, I have found the characteristic firm, round or oval encapsulated angioma only twice in examining about 2,000 specimens. While angiomas do not usually exceed from 1 to 2 cm. in diameter, much larger ones have been reported. The tumor may be shelled out of its pseudocapsule very much like a fibroid tumor of the uterus. Microscopically it is made up of innumerable small crowded capillaries, apparently within the confines of the stretched out Langhans and syncytial boundary of the original villus. Angioma is of no significance unless large enough to induce premature labor or possibly cause dystocia.

Conversely, if the villi fail to be vascularized or are insufficiently vascularized, degenerative changes of a hydropic nature may occur in the stroma and the lining cells which may possibly account for hydatidiform mole. One observes a similar tendency to edema of the villi, with the failing vascularity incident to syphilis of the placenta. In hydatidiform mole, however, the process is not a simple edema affecting the villous stem uniformly throughout but is a hydropic degeneration localized in a succession of enlargements along the course of the stem, giving rise to grapelike clusters of thin-walled cysts, which add immensely to the size and weight of the placenta and tend to loosen it from the uterine wall.

Embryonic growth is interfered with at a very early stage, and one seldom finds any trace of embryo or normal placental tissue. The Aschheim-Zondek test is strongly positive, because of increased concentration of the hormone. Enlargement of the ovaries, due to lutein cyst formation, frequently occurs and may be due to overstimulation of the anterior lobe of the pituitary gland from the excessive growth and degeneration of the epithelial elements of the villi. The enlargement subsides rapidly after expulsion of the mole.

The site of attachment and embedding of the fertilized ovum determines the location of the placenta in the uterus. While this is apparently largely a matter of chance, the vast majority of implantations are on the anterior or posterior wall of the fundus or body of the uterus.

Implantation in the lower uterine segment, resulting in placenta praevia, occurs much more frequently in multiparas. Is it not possible that the explanation of this lies in the fact that the anterior and posterior walls of the parous uterus are separated more than those of the virgin uterus, thus permitting the blastocyst to gravitate to a low level before embedding?

It would be of interest to compare the incidence of placenta praevia in a large series of cases in which the uterus is known to have been retroverted early in pregnancy with that in a like number of cases in which the uterus is known to have been in normal anteversion early in pregnancy.

Variations from the usual oval or round shape of the placenta probably result from lateral or cornual implantation. It is possible, however, that persistence of chorionic villi which unexpectedly survive their unfavorable location over the chorion laeve may account for some of the irregularly shaped placentas or the islands of placental tissue sometimes seen on the membranes and termed placenta membranacea.

During the second and third trimesters of pregnancy, with increasingly frequent and strong Braxton Hicks contractions and trauma, both from fetal movements within the uterus and stimuli from without, some of the outermost fastening villi at the margin of the placenta are probably torn from their decidual bed, thus

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causing repeated slight extravasations of blood at the margin of the placenta. The blood is prevented from extending inward beneath the placenta by the denser, more secure fastening villi or outward by the adherence of the membranes to the uterine wall. Consequently it follows the path of least resistance and bulges the chorion and amnion inward over the fetal surface of the placenta. This bulging fold of chorion and amnion, with its contained blood, is gradually flattened down onto the margin of the placenta by the intra-amniotic pressure.

After absorption of the hemoglobin the remaining fibrin creates the appearance of a thickened yellow border around part or all of the circumference of the placenta. This is, according to my observations, the probable mode of origin of circumvallate placenta. A section through the margin of such a placenta should show, from without in, (1) placenta, (2) chorion, (3) amnion, (4) amnion, (5) chorion, (6) fibrin, (7) chorion and (8) amnion. It is difficult, however, to identify and trace each of these layers in a specimen. The circumvallate border apparently opposes the further outward course of the vessels on the fetal surface of the placenta; these are seen to dip into the substance of the placenta at the inner margin of the circumvallate ring and continue their course within the placental substance to the extreme rim of the placenta, which in some cases extends several centimeters beyond the circumvallate ring.

In the last half of pregnancy certain changes occur in the placental arteries which play an increasingly important part, predisposing to hemorrhage and infarction. The basis for the vascular changes is the hypercholesteremia of pregnancy, which, from the early months on to term, is probably of fundamental importance to fetal growth.

Cholesterol, in the language of the biochemist, has been termed the framework of the body cell. If it is, there must be some mechanism by which the maternal organism mobilizes cholesterol to supply the excessive demands of cell growth in the fetus. It is thought that the pituitary gland governs cholesterol metabolism, and stimulation of the various functions of this gland by pregnancy may explain the mechanism by which the value for blood cholesterol increases from a normal one of from 150 to 170 mg. to an excessive one of from 200 to 250 mg. or more per hundred cubic centimeters. This value is still further increased if there is associated hypothyroidism or if the diet is particularly rich in cholesterol-containing foods.

Another factor, which, independently and also in conjunction with the hypercholesteremia of pregnancy, lays the basis for vascular changes in the placental arteries, is trauma produced by the increasingly vigorous movements of the fetal extremities on the unprotected vessels on the fetal surface of the placenta in the latter part of pregnancy. In respect to vulnerability, lack of support from surrounding tissue and subjection to direct trauma, the placental circulation is unique and unlike that of any other part of the body.

Under the combined influence of hypercholesteremia and fetal trauma, focal collections of lipoid-like cells arise beneath the endothelium in some of the smaller placental arteries, probably at points where the vessel has been traumatized. I [1] noted the similarity in appearance of these focal accumulations of lipoid-like cells in the smaller placental arteries to the experimental cholesterol-induced vascular changes in rabbits and the spontaneously occurring vascular change accompanying coronary thrombosis in man, as shown by Leary.[2]

The accumulation of lipoid cells beneath the endothelium and in the vessel wall may disturb the circulation in either of two ways. The lumen of the vessel may be gradually narrowed by bulging of the focus of lipoid cells, which may finally shut off the circulation to the dependent villi, or the endothelium overlying the lipoid cells may break down, either spontaneously or from the trauma of fetal movements, thus causing sudden thrombosis and loss of blood supply to the villi. Infarction necessarily follows, progressing rapidly in case of thrombosis or more slowly in case of mere narrowing of the lumen.

Areas of acute infarction in the placenta and their association with toxemia of pregnancy were first emphasized by Young.[3] He, however, considered them to be the result of interruption in the maternal blood supply, a view which cannot be reconciled with the sinusoidal character of the intervillous circulation. Manifestly, loss of maternal blood supply to any part of the placental site cannot deprive adjacent villi of maternal blood, which is free to reach this area from the surrounding intervillous circulation. Furthermore, villous vessels in the infarcted area are found to be thrombosed, indicating that the cause is on the fetal rather than the maternal side of the circulation.

Placental infarcts have been attributed also to the effect of some unknown toxic substance in the maternal circulation which causes localized degeneration of the villi. In view of the sharp line of demarcation between necrotic villi within the infarcted area and the surrounding healthy villi just beyond the border of the infarct, and the open intervillous circulation common to the two areas, it is inconceivable that any maternal poison circulating freely throughout the intervillous spaces would show a selective action on certain areas and not be uniformly harmful to all villi.

Failure to appreciate the relationship between placental infarcts and toxemia of pregnancy has been due to improper preparation and examination of the placenta and lack of familiarity with the more acute types of placental infarcts. The placenta should be wiped free of blood, the membranes cut away from the margin and the specimen fixed in 10 per cent solution of formaldehyde for from three to four weeks. It should then be cut in strips from 0.5 to 1 cm. thick, which are closely examined for evidence of infarction or hemorrhage.

Previous to 1937 I followed a routine of examining placentas in the light of a knowledge of the clinical history of each case. One cannot avoid being influenced in his interpretation of a suspicious area if he knows in advance whether or not the patient has had toxemia. During the past year all examinations have been made on "unknown" placentas, without a knowledge of the patient's clinical history at the time the placenta was sectioned. A definite diagnosis as to the occurrence of toxemia during the pregnancy has been made on the basis of the gross pathologic changes and then compared with the clinical diagnosis.

1. Bartholomew, R. A., and Kracke, R. R.: Am. J. Obst. & Gynec. **31**: 549 (April) 1936.

2. Leary, Timothy: Experimental Atherosclerosis in the Rabbit Compared with Human (Coronary) Atherosclerosis, Arch. Path. **17**: 453 (April) 1934.

3. Young, J.: J. Obst. & Gynaec. Brit. Emp. **26**: 1, 1914; **34**: 279, 1927.

By this method it has been possible to arrive at a much more accurate classification of placental lesions and establish criteria and characteristics which differentiate the acute from the subacute or more chronic types. In a recent publication [4] placental infarcts were classified as A, *B*, *C*, *D* and *E*, listed in the order of increasing rapidity of infarction as well as in the order of increasing toxicity. The italicized letters indicate the infarcts which are associated with the increasing degrees of toxemia.

If infarction occurs rapidly the affected placental tissue appears as one or more round or oval areas

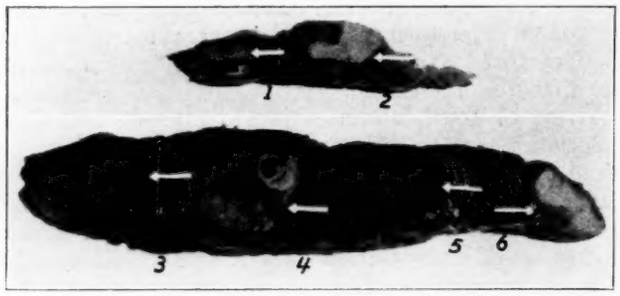

Fig. 1.—Placental strips from a primigravida, aged 21, who was normal at the twenty-seventh week of pregnancy but showed edema, slight albuminuria and a blood pressure of 150/82 at the thirtieth week, with no apparent increase at the thirty-second week. Two weeks later eclampsia and abruptio placentae developed; the blood pressure was 152/108 and increased to 170/130, and there was heavy albuminuria. Pregnancy was terminated and the patient recovered. Diagnosis from this placenta, sent from Dr. N. J. Eastman's service, Johns Hopkins Hospital, and examined as an "unknown," was as follows: Infarct *C* (1) and *B* (2) were probably responsible for a gradually increasing toxemia of several weeks' duration, followed by an acute exacerbation with severe toxemia and abruptio placentae due to early *D* (3), late *D* (4) and early *E* (5) infarcts. A late *D* infarct (4), with a superimposed blood clot, was responsible for the abruptio placentae. Infarct A (6) is nontoxic.

from 1 to several centimeters in diameter, which are sharply demarcated from the surrounding normal placental tissue by the color, which is a dark purple-black. These areas correspond to the distribution of the obstructed vessel. The consistency is still spongy and soft, as in normal placental tissue. When the strip is held toward the light the infarcted area preserves a granular-appearing surface. When the strip is bent the infarcted area bends as easily as the normal tissue. There may be a soft or a firm clot within or adjacent to the area. This type of infarct is designated as the early *E* infarct (figs. 1 and 2).

Microscopically, the stroma and lining cells of the villi show pyknosis and early karyolysis and are somewhat swollen, because of congestion of the villous capillaries. Many villous capillaries are thrombosed or show marked distention and rupture, with extravasation of fetal blood into the intervillous spaces, which accounts for the soft or firm clot. The intervillous circulation is freely open, there being no evidence of thrombosis.

Biochemically, placental tissue has been found to contain relatively more arginine than any other tissue.[5] Theoretically, in the process of autolysis of the infarcted area, guanidine may result from the breaking down of arginine [6] and, since guanidine is known to produce convulsions, the peculiar eclamptogenic nature of placental autolysate may thus be explained. Kracke, in testing the effects of injection of autolysates of various tissues into animals to stimulate leukocytosis, has never observed convulsions, although toxic effects are evident.

Other poisonous protein split products resulting from placental autolysis are probably peptone and histamine. Peptone, if present in sufficient concentration, inhibits thrombosis through its anticoagulant effect. This tends to keep the intervillous circulation open and permits absorption of the poisons into the maternal circulation. The known effects of these products explain practically all the clinical and pathologic manifestations of toxemia of pregnancy.

Clinically, the acute type of infarction is associated with the more acute, fulminating, preeclamptic, eclamptic or abruptio placentae type of toxemia, and there is a direct relation between the amount of tissue involved and the severity of the toxemia. It is usually found when the patient progresses from a normal state to preeclampsia, eclampsia or abruptio placentae within a week or ten days.

If infarction is slightly older or less acute (late *E* infarct, fig. 2) the lesion is still dark or purple-black but has changed from a spongy to a more compact firm area, sharply demarcated from the surrounding lighter spongy tissue. It is firmer to palpation, and when the strip is held toward the light the surface of the lesion appears marble-like and shiny. When the strip is bent, the infarcted area either cracks sharply or holds together and does not bend with the rest of the strip.

Microscopically, the villi show pyknosis and some degree of karyolysis and karyorrhexis. Some of the distended villous capillaries are ruptured and the extravasated blood, with tissue débris, fuses the villi and causes the area to appear more compact. There is still open intervillous circulation, which disseminates poisonous protein split products of placental autolysis. Clinically, the toxemia is almost if not quite as fulminating as that associated with the early *E* infarct, but there may be opportunity to induce labor before abruptio placentae or eclampsia occurs.

If infarction is still less acute or of longer duration, corresponding to a clinical course of from two to three

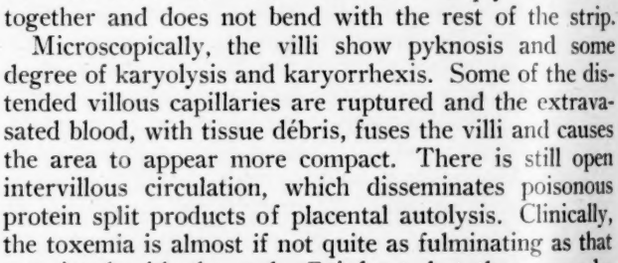

Fig. 2.—Placental strips 3 and 4 were obtained from patients with eclampsia and preeclampsia, respectively. The arrows point to two late *E* infarcts (1) and early *E* infarcts (2, 3, 4 and 5).

weeks, the infarcts vary from a faint brown (early *D*) to a definite brown (late *D*), as seen in figure 1, and are sharply demarcated, firm, compact, smooth and shiny and hold together when the strip is bent. Microscopically, the blood cells, both maternal and fetal, are more degenerated and stain more faintly, the change in the hemoglobin accounting for the brown color. The villi show more necrosis and disintegration. The inter-

4. Bartholomew, R. A., and Colvin, E. D.: Tr. Am. Gynec. Soc., June 1938; Am. J. Obst. & Gynec. **36**: 909 (Dec.) 1938.
5. Harding, V. G., and Fort, C. H.: J. Biol. Chem. **35**: 29 (July) 1918.
6. Bartholomew, R. A., and Parker, Francis: Am. J. Obst. & Gynec. **27**: 72 (Jan.) 1934.

villous spaces are still open and permit free absorption of toxic autolytic products.

In a series of 100 placentas, from both normal and toxic patients, examined as "unknowns," [4] there were twenty which suggested severe toxemia, classified clinically as preeclampsia, eclampsia and abruptio placentae. The presence of early and late types of infarcts *D* and *E* made it possible to make a correct pathologic diagnosis in 90 per cent of the cases.

If infarction is even slower the lesion, designated as infarct *C* (fig. 1), appears as a brown-yellow, sharply demarcated area and may show some softening or breaking down. Microscopically, the villi stain poorly or not at all and show considerable disintegration. The intervillous circulation is sufficiently open to permit absorption of toxic products, but there is considerable intervillous thrombosis in some parts of the infarct. Clinically, infarct *C* is associated with toxemia of a more gradual but progressive type, extending over a period of four or five weeks. Induction of labor may be necessary.

Infarct *B* (fig. 1) is a slow-forming, yellow-white, firm, sharply demarcated lesion and is apparently due to gradual obliterative endarteritis or slow occlusion from cholesterol-induced vascular change. Since the small arteries are more often affected, the infarct is usually found on the margin of the placenta.

Microscopically, the villi are pale and stain faintly but preserve their normal outline. There is no disintegration. The thrombosed intervillous blood has been changed to a dense homogeneous pink-staining hyaline substance, but in some areas there is still slight intervillous circulation. The yellow color of the lesion is due to scattered areas of incomplete thrombosis, containing shadows of degenerated red cells and some active necrosis of the villi, which permit slight absorption of toxic products.

Clinically, infarct *B* is associated with very mild manifestations of toxemia. The patient may have had slight edema, a trace of albumin and a slight rise in diastolic blood pressure, to 80 or 85, but there has been no tendency to increased toxemia unless a new area of more acute infarction occurred.

Infarct A (fig. 1) is firm and sharply demarcated and appears identical with infarct *B* (fig. 1) except that it is white. The absence of yellow color is due to complete hyalinization of the intervillous blood which surrounds the pale "ghost villi." Since the etiologic factor is slow obliterative endarteritis in a terminal artery, infarct A is usually on the margin of the placenta. It is nontoxic, not only because of the complete hyalinization of the intervillous blood but also because of the slow necrosis of the affected villi.

Lesions A, *B*, *C*, *D* and *E* are true infarcts characterized by progressive increase in the rapidity of infarction. Grossly, the more rapid the infarction the less conspicuous the lesion, the less firm the consistency, the darker the color and the greater the toxicity. Microscopically, the more rapid the infarction the less apparent the intervillous thrombosis and, except in the most acute stage, the greater the disintegration and loss of staining power of the villi. The range in color, due to change in the hemoglobin, is from very dark purple-black in infarct *E* to brown in *D*, to brown-yellow in *C*, to yellow-white in *B* and to white in A. The size and number of the infarcts bear a definite relation to the severity of the toxemia.

Simple hemorrhage without associated infarction may also occur in the placental substance. Since there can be no hemorrhage in a sinusoidal circulation such as the intervillous circulation, the probable source of such hemorrhage, when there is no associated infarction, is simple rupture of the capillaries of a terminal villus, resulting in extravasation of fetal blood. The villi are forcibly pushed aside and compressed about the margin of the hemorrhage.

Whether the collection of blood is absorbed and drained away completely, leaving an excavated open area, or whether a blood clot remains and passes through the stages from dark to brown clot and finally to white or yellow fibrin probably depends on the compatibility of the maternal and fetal blood. A slight degree of incompatibility may account for the soft transparent gelatinous areas which are occasionally seen in the placental substance. Shadows of red cells or a slight pink color give evidence of a hemorrhagic origin of these areas.

A layer of compressed villi about a recent hemorrhage may simulate an acute infarction, particularly if there is some infiltration of dark blood into the villi beyond the hemorrhage, thereby giving to the area a dark color. The lesion, however, is diffuse and not sharply demarcated. Microscopically, the villi do not show necrosis. If the clot is yellow or white the evident age of the hemorrhage argues against an associated acute infarction and the compressed border of the lesion is of a lighter color owing to crowded villi and diminished intervillous blood.

The cause of simple hemorrhage in the placental substance is obscure, but it seems reasonable to believe that temporary pressure on the thin-walled umbilical vein through certain movements or positions of the fetus in the late months of pregnancy may cause sufficient distention of a terminal villous capillary that rupture may occur.

Small collections of yellow-white fibrin varying from 0.5 to several centimeters in diameter are frequently seen on the fetal surface of the placenta beneath the chorion. The origin of these lesions is undoubtedly rupture of small branches of the umbilical arteries from the trauma of fetal movements. They are occasionally of immense size, indicating sudden extravasation from rupture of a large artery.[7] Cysts on the fetal surface of the placenta undoubtedly arise from liquefaction of a localized hemorrhage.

The circulatory disturbances thus far described concern pathologic changes in the placental arteries. I believe that the rare fetal anomaly termed general edema of the fetus, concerning which Ballantine wrote a monograph, is due to occlusion of the umbilical vein at some point between its origin at the placental end of the cord and its tributaries in the liver within the body of the fetus. The condition is associated with a high incidence of toxemia and marked increase in size of the placenta, which appears pale, white and extremely edematous. The villi show marked edema and early degenerative change due to slowing or arrest of the circulation. Since the entire placenta is involved, the toxemia is acute and severe. There is urgent need to investigate cases of general edema of the fetus, particularly from the standpoint of this probable etiologic factor. The frequency of fetal blood dyscrasia, with

7. Bartholomew, R. A., and Kracke, R. R.: Am. J. Obst. & Gynec. 24: 797 (Dec.) 1932.

excessive numbers of megaloblasts, emphasizes the importance of a complete study of the blood.

Finally, local or general infection of the placenta may occur by way of the genital tract or through the maternal blood stream. Pyogenic infection is practically always postabortal and ascending by way of the genital tract. Portions of the decidua and the adjacent intervillous spaces show thrombosis and numerous polymorphonuclear leukocytes. Invasion of the fetal circulation by the organisms, and intra-uterine fetal death, while apparently rare, may prove to be more frequent than suspected with closer study of the placenta and improved methods of isolation of bacteria from the fetus.

Tuberculous infection of the fetus is necessarily transplacental and is generally believed to be preceded by definite tuberculous lesions of the placenta. The demonstration of tubercle bacilli may require thorough search by histologic and inoculation methods. However, the finding of tuberculous lesions in the placenta does not invariably mean that the fetus is infected.

Syphilis of the placenta, contrary to statements frequently made in the literature and textbooks, is not recognizable by a specific appearance of the gross specimen and is not always suggested by undue size of the placenta. Microscopically, in the more mature placentas of the last trimester of pregnancy the villi appear large, somewhat crowded and edematous. The stroma shows rather loose open structure, and the vessels of the villi are inconspicuous in number and size and show round cell infiltration. Spirochetes are demonstrated with much more difficulty in the placenta than in the fetus. A positive histologic appearance is strong evidence of syphilis but is not regarded as positive proof.

Since the placenta apparently functions as a rather efficient barrier to transplacental infection of the fetus, some experiments were carried out by Kracke to determine if possible whether placental extract, in comparison with other tissue extracts, possesses some bactericidal power or inhibiting influence on bacterial growth when used as a culture medium. Contrary to the anticipated result, it was found to be a good culture medium for the commonly occurring bacteria and an excellent medium for streptococci.

CONCLUSIONS

1. Infarction of the placenta is the most important pathologic condition to which this organ is subject, not only from the standpoint of frequency but also because of its relation to toxemia of pregnancy and maternal and fetal mortality.

2. The predisposing causes of placental infarction are, first, the hypercholesteremia of pregnancy, which favors the accumulation of lipoid cells at points of stress or injury of the placental arteries, similar to that seen with coronary occlusion, and, secondly, the trauma of fetal movements, which not only tends to cause deposits of lipoid cells at points of injury to the placental arteries but also may break the endothelium over such a deposit or actually bring about rupture of the vessel, thus causing rapid thrombosis.

3. Toxemia of pregnancy probably results from the absorption of poisonous protein split products of placental autolysis.

4. The poisonous products of placental autolysis are probably peptone, histamine and guanidine. The pathologic effects of these poisons satisfactorily explain the symptoms and pathologic changes of toxemia of pregnancy.

5. The peculiar eclamptogenic character of placental autolysate is probably explained by the higher content of arginine in placental tissue, from which guanidine may be obtained.

6. Toxemia of pregnancy is associated with definite types of acute infarction of the placenta. In examining "unknown" placentas it is possible to diagnose preeclampsia, eclampsia or abruptio placentae in 90 per cent of the cases.

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ABSTRACT OF DISCUSSION

DR. A. J. CARLSON, Chicago: I presume these placentas were taken in a routine manner. Did you examine all the placentas?

DR. BARTHOLOMEW: That is right.

DR. CARLSON: What is the amount of guanidine in the urine in these patients? There have to be considerable amounts in the blood to get these symptoms. What about the pathologic conditions in the liver that have been described in these eclamptic patients? Do you describe them as secondary effects of these poisons from the placenta?

DR. FRANK W. HARTMAN, Detroit: I had the privilege a few years ago of reviewing a thousand consecutive placentas at our hospital, and we found over 50 per cent of infarcts. We were unable to correlate in any way the number or size or occurrence of these infarcts with toxemias in this group of cases. I wonder if the infarcts in the placenta aren't the result of the same thing that produces the liver lesions and other lesions throughout the body rather than that the infarcts produce the chemical changes that are the initial cause. There is some substance which produces the spasm, perhaps, of the vessels, and the infarcts in the placenta, and the hypertension and the changes in the liver. It has been shown that one of the best ways to reproduce these lesions in the liver is to place animals under partial oxygen tension for several days, and under those conditions of anoxia the liver does show lesions very close to the lesions seen in the toxemia of pregnancy. Another condition in which similar facts have been blamed for shock and death is extensive burns. There the blood pressure goes in the opposite direction, it usually falls, and the patient dies from vascular collapse and shock. They frequently show lesions in the liver which are very similar to what are seen in eclampsia.

DR. R. A. BARTHOLOMEW, Atlanta, Ga.: With regard to whether guanidine is present in the urine, we have not finished some work that has recently been undertaken, namely, taking an equal weight of placenta and liver or spleen, and subjecting both tissues to autolysis to determine if possible whether there is a greater amount of guanidine obtainable from placental tissue. Major, I believe, has demonstrated an increased amount of guanidine in the urine of eclamptic patients and Titus has produced convulsions and eclamptic-like lesions in the liver and kidney of rabbits by injections of guanidine. In the early part of the work guinea pigs were injected with autolysate of human placenta which had autolyzed as little as four or five hours, and daily injections over a period of eight or ten days resulted in the production of typical eclamptic convulsions and a pathologic condition of the liver and kidney similar to that seen in eclampsia. I emphasized particularly that acute placental infarcts are sharply circumscribed and that the intervillous circulation in the infarcted area is widely open, permitting maternal blood which circulates freely in the adjoining healthy placenta to circulate between the necrotic villi of the infarcted area. The acute infarcts cannot be explained on the basis of a hypothetic poison in the maternal blood. Such a poison would have a uniformly lethal effect on all villi and not a selective effect in certain areas of the placenta. This, in my opinion, indicates that the infarct and its poisons are primary in the placental tissue and not in the mother's blood.

THE USE OF POTASSIUM SALTS IN HAY FEVER

PRELIMINARY REPORT

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TUCSON, ARIZ.

The present study was stimulated by the thought that allergy is, in great part, a disturbance of electrolyte metabolism. Analogy could be drawn between demonstrated electrolyte disturbances in other diseases, such as thyroid disease (iodide), parathyroid disease (calcium), Addison's disease (sodium and potassium) and the potassium alterations that have been described in diabetes.

Cook and Stoesser [1] treated asthmatic children with "salt-free" diets and injections of pitressin and found that, in spite of the antidiuretic action of the pitressin, there was an increased, rather than a decreased, excretion of the sodium ion and that with this there was a distinct relief of the asthma. In one patient asthma was seemingly reinduced by the administration of a large dose of sodium chloride. This experimental work also suggests the importance of the water balance in asthma, comparable to its importance [2] in Addison's disease. Clinically, Piness [3] has stressed the importance of the need for water by patients with status asthmaticus, and he therefore administers it by various routes in copious amounts in these cases. Davis [4] has had remarkable success in the treatment of chronic asthma by a regimen an important part of which is the free use of water enemas.

In the article by Rusk and Kenamore [5] the excellent suggestion was made that urticaria might be an expression of localized edema which might respond to the action of a diuretic. They used potassium chloride and found it thoroughly effective in six cases of severe urticaria. They quote Nathan and Stern [6] as saying that in the acute dermatoses serum potassium fell to a subnormal level and returned to normal as the cutaneous lesions improved.

It has been demonstrated that the pharmacologic action of potassium chloride is, in many respects, similar to that of epinephrine. Seager,[7] however, could not verify this similarity in the iris of the frog. In addition, in my own experiences with potassium chloride none of the usual side-effects of epinephrine or ephedrine were observed in the doses used (the highest dose being 50 grains [3.3 Gm.] in twenty-four hours), in spite of its effectiveness and at times surprisingly rapid action. Rusk and Kenamore state that "effects attributed to epinephrine are actually the effects produced by potassium migration which epinephrine causes." This would readily explain the well known ineffectiveness of epinephrine in status asthmaticus after repeated, frequent doses have been given. In other words, epinephrine liberates potassium from the tissues, and when the tissues are sufficiently depleted epinephrine can no longer relieve the symptoms of allergy.

CLINICAL RESULTS

This preliminary report deals mainly with the use of potassium salts in a number of patients with hay fever. The clinical results shown in the accompanying table appear to be so conclusive that lengthy, detailed reports of cases will be omitted.

The method of administration proved to be simple. In one of the first cases in which potassium chloride was tried it was given as a 10 grain (0.65 Gm.), enteric coated capsule. This produced agonizing epigastric pain five minutes after administration and later, when it was found that other patients complained of vague abdominal distress, it was decided to give it in 5 grain (0.32 Gm.) doses dissolved in a glass of water. This illustrates the need for extensive studies on the toxicity of potassium salts, although the latter procedure proved to be entirely satisfactory. Later, when it was felt necessary to prove that the clinical effect came not from potassium chloride as such but from the potassium ion, a mixture of potassium salts in solution was prescribed, and this was found to be almost equally effective. This solution of potassium salts contained 3⅓ grains (0.2 Gm.) each to the drachm (4 Gm.) of potassium acetate, potassium bicarbonate and potassium citrate. Rusk and Kenamore experienced no real difficulty with the use of 15 grain enteric coated capsules, but in view of my experience I would recommend that these salts be given in dilute solution. A 5 grain powder of potassium chloride dissolved in a glass of water is practically tasteless.

The Effect of Potassium Salts on Hay Fever and Pollen Asthma *

Case	Age	Sex	Diagnosis	Severity	Relief Obtained
1. M. T.	36	♀	Hay fever	+++	++++
2. P. B.	39	♂	Hay fever	+++	++++
3. E. R.	24	♀	Hay fever	++	++++
4. E. S.	44	♂	Hay fever	+++	++++
5. F. B.	38	♀	Hay fever	+++	++++
6. W. C.	42	♂	Hay fever	++	++++
7. R. W.	43	♀	Hay fever	+++	++++
8. S. W.	44	♂	Hay fever	+	++++
9. W. P.	41	♂	Hay fever	+	++++
10. M. R.	40	♀	Hay fever	++++	+++
11. D. W.	18	♀	Hay fever	+	+++
12. M. M.	40	♀	Hay fever	++++	++++
13. W. R.	38	♂	Hay fever	++	+++
14. E. R.	37	♀	Hay fever	++++	++++
15. L. W.	30	♀	Hay fever	+++	++++
16. J. B.	16	♂	Hay faver	+++	++++
17. L. G.	37	♀	Hay fever	++	++++
18. D. M.†	42	♂	Hay fever	+	+++
19. B. D.	40	♀	Hay fever	+++	++
20. M. L.	31	♀	Hay fever	++++	++++
21. B. B.†	37	♂	Hay fever	+	++++
22. O. H.	44	♂	Hay fever	++++	++++
23. F. N.	38	♀	Hay fever	++	++
24. A. A.	33	♀	Hay fever and asthma	+++	+++
25. J. T.	12	♂	Hay fever and asthma	++++	++++
26. S. L.†	32	♀	Hay fever and asthma	+	++++
27. E. M.	12	♂	Hay fever and asthma	+++	++
28. F. I.	28	♀	Hay fever and asthma	+++	++
29. S. Q.	19	♀	Hay fever and asthma	++	++++

* Most of these patients were originally treated with 5 grains of potassium chloride three times a day; in a few cases four doses were given; the most that one patient received was 50 grains (3.2 Gm.) a day. The doses for children and the elderly must be worked out.

† These patients had had nearly adequate relief from desensitization.

Read at the regular meeting of the Pima County Medical Society, Nov. 15, 1938.

Dr. Solomon Strouse, Los Angeles, and Dr. Donald F. Hill, Tucson, encouraged and assisted in this work.

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2. Personal communication to the author from Dr. H. H. Cutler, Rochester, Minn.
3. Personal communication to the author from Dr. George Piness, Los Angeles.
4. Personal communication to the author from Dr. W. Claude Davis, Tucson, Ariz.
5. Rusk, H. A., and Kenamore, B. D.: Urticaria: A New Therapeutic Approach, Ann. Int. Med. **2**: 1838 (April) 1938.
6. Nathan, E., and Stern, F., quoted by Rusk and Kenamore.[5]
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Hay Fever.—Altogether twenty-nine cases of hay fever, six with pollen asthma, were studied during the Tucson fall hay fever season, the common offenders at that time being false ragweed, careless weed (amaranth) and bermuda grass. The symptoms varied in severity from slight sneezing and nasal discharge to severe hay fever symptoms and, in the six cases, asthma. Most of the patients responded quickly to 5 grains of potassium chloride given three times a day, some experiencing relief within a few minutes and some in about a half hour. Others, whose hay fever was mostly nocturnal, reported the next day that they had had much better nights. In only one case did an increase of symptoms follow an initial improvement, and this patient obtained adequate relief after the dose was increased to 25 grains (1.6 Gm.) of potassium chloride a day.

In one family of four, all of whom had severe hay fever, the two who were given the medicine responded; the other two continued to have hay fever. In another family of three sisters, all with severe hay fever, the one who was given the medication obtained complete relief; the other two continued to have severe hay fever. In the series of hay fever cases control studies by substituting inert medication were not carried out. One patient had a return of symptoms within twelve hours after he stopped taking his medicine and was again relieved as soon as it was resumed. In one case the medication was experimentally stopped and symptoms returned the following day; medication was resumed after three days and the symptoms disappeared satisfactorily. In a few instances, patients neglected to take their potassium chloride regularly and found that the omission of one dose resulted in a recurrence of symptoms, usually in from five to eight hours.

As is indicated in the table, every one of the patients experienced a degree of relief which in all cases was estimated as over 50 per cent and in most of them approximated 100 per cent. The first improvement noticed was the disappearance of irritation of the eyes. Within twenty-four hours the copious nasal discharge had almost entirely cleared. For about another day a few of the patients persisted in having a rare attack of dry sneezing. By the third day the patients who in the table are graded as having a 4 plus relief were free from symptoms. With the disappearance of sneezing and discharge, which in many cases interfered with sleep, the general state of health of these patients was greatly improved.

The following report illustrates the striking effect of potassium chloride in a severe case:

J. T., a boy aged 12 years, had had hay fever and asthma for the past eight summers, during the last four of which considerable relief had been obtained by desensitization with an allergen mixture. Injections had been omitted the past summer because of the illness of the patient's physician. The summer was spent on the Pacific coast, where the boy was practically free from symptoms. On returning to Tucson, however, during the ragweed and careless weed seasons, hay fever and then asthma started, and as these increased in severity diarrhea, abdominal cramping and then vomiting set in. In ten days the boy lost 15 pounds (6.8 Kg.). The patient could have been treated with epinephrine and ephedrine, or he could have been moved into a pollen-free atmosphere. It was decided, however, to try potassium chloride. The first dose was immediately regurgitated; half an hour later another dose was given and from that time on there was no sneezing, wheezing or vomiting. By the next day the cramping and diarrhea had disappeared. The medication was continued in 5 grain doses three times a day. At the end of a week he had regained about 10 pounds (4.5 Kg.) and felt fine.

The only complicating factor in this series was in case 28. This patient had not only hay fever and asthma but also urticaria, rheumatic heart disease and a long-standing, persistent, mild arthritis. This patient became entirely free from hay fever and asthma for two days but then had recurrent asthma and urticaria thought to be due to food sensitivity. This case will be reported in detail later.

Chemical studies of blood and urine, which had been done on the chronic asthmatic patients and which will be reported later, were not made in this group of hay fever patients.

Chronic Asthma.—The original studies on this phase of allergy were made on a group of ten patients with chronic persistent asthma. It is important to note that in none of them did any improvement occur from potassium chloride. Studies on these patients are being continued and will not be reported here in detail. It is sufficient to say that I have found in these cases that a "salt-free" diet seemingly decreases the severity of the asthma and that, furthermore, the administration of potassium iodide during the period of the "salt-free" diet practically eliminates severe asthmatic attacks. The beneficial effect thus obtained seems to be greater than would be obtained by the use of a "salt-free" diet or of potassium iodide alone. It should be made clear that these patients are, in general, not cured, although some of them are much better than they were before treatment was started.

Other Allergic Diseases.—In view of the excellent results obtained with hay fever it was thought advisable to record the results obtained in a small number of cases of other allergic diseases. Three cases of urticaria, two chronic and one acute, responded favorably to 5 grain doses of potassium chloride given three times a day. The skin in one case of long-standing thickly encrusted eczema was almost cleared in five days, leaving at that time only a brown-red discoloration to the smooth skin. In another case a mild eczematoid, itching lesion of the forearms disappeared in three days. Three patients with chronic sinusitis, apparently allergic, reported decrease of discharge and pain. In one of these acute severe frontal and antral pain completely disappeared in three minutes. In one patient with nasal polyps which had completely blocked the passage of air on both sides for three weeks, opening of the air passages occurred within an hour after a 5 grain dose of potassium chloride. The patient had expected to have nasal polyps removed, as had been done in the past, but has had practically no nasal blocking since this one simple experiment was tried three months ago. A Negro woman with nasal polyps completely blocking both nares was kept on potassium chloride 5 grains three times a day for two weeks, at the end of which time the polyps on the left side were seen to have partially shrunk, so that the anterior third of the left naris was free. One week later the left naris was sufficiently open to permit the passage of air. The results in these two cases encourage the belief that even severe nasal polyposis does not inevitably require surgery. In another instance, in which nasal polyps had recently been removed, potassium chloride was given and after two days the patient noticed marked freeing of the air passages. Dr. John Mikell, nose and throat specialist, who was unaware of the nature of the medication or of its mode of action, found at this time that the edema of the inferior turbinate had completely disappeared. In three typical cases of migraine relief

was obtained in only one, and this occurred within four hours after 20 grains (1.3 Gm.) of the potassium salt mixture was given. In two other cases no effect was produced with 15 grain and 30 grain (1 and 2 Gm.) doses of potassium chloride respectively.

It must be emphasized that these results are in no way to be considered conclusive. They are reported here only because, in some instances, various allergic disturbances seem to respond to potassium salt therapy.

Food Sensitivity.—A simple clinical experiment was tried on a man aged 44, who had for years regularly had acute nasal blocking (from polyps) and severe hives following the ingestion of shrimp, beer, candy in large amounts, or a combination of tomatoes and sugar, for each of which substances he had a penchant. He was asked to eat a portion of shrimp after taking 5 grains of potassium chloride. In his enthusiasm for the experimental method he took not only a large portion of shrimp but also a glass of beer, some tomatoes and sugar and then a large quantity of candy. No hives appeared but some rhinitis did develop, which was quickly relieved by the second dose of the medicine. The following morning he ate three tablespoonfuls of jam, which had also always given him hives and nasal blocking but which this time produced no symptoms at all.

COMMENT

From the results obtained in this study, as well as those reported by Rusk and Kenamore, it seems that potassium plays an important role in the mechanism of allergy. Obviously other electrolytes, including sodium, calcium, chloride and iodide, take part in this complex disturbance. Much recent work has shown the importance of altered electrolyte metabolism in endocrine disturbances, and it may well be that allergy is basically an endocrine dysfunction with secondary disturbances of electrolyte metabolism. This hypothesis, however, remains to be demonstrated. In view of the good results obtained in a few cases of asthma and eczema, with adrenal cortex extract, and in view of the known relationship in Addison's disease of the adrenal cortex to sodium and potassium disturbance, it seems probable that it is the adrenal gland that is primarily involved. Because of the well established relationship of epinephrine to allergic manifestations it would seem that this disturbance of the adrenal gland involves the medulla as well as the cortex.

This concept of allergy, indicating that the major disturbance is one of altered electrolyte metabolism, immediately suggests that the proteins produce manifestations only when the underlying electrolyte mechanism is disturbed.

It has been shown in this study that a much neglected simple inorganic chemical compound is of considerable importance not only in therapy but also in the study of a complex group of disturbances. It is hoped that this work will stimulate others whose facilities are more adequate.

CONCLUSIONS

1. Striking benefit was obtained from the use of potassium salts in twenty-nine cases of hay fever. These salts are also used in urticaria, eczema, nasal polyposis, chronic allergic sinusitis and migraine.

2. In chronic asthma potassium chloride is apparently ineffective; the use of potassium iodide, however, in combination with a salt-poor diet, seems helpful but not curative.

3. The method of administration of potassium salts is simple; no complication or "side effects" were noted, although further studies of toxicity are needed.

4. It is suggested that allergy is predominantly a disturbance of electrolyte metabolism associated with some endocrine (possibly adrenal) dysfunction.

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TOXIC HEPATITIS DUE TO SULFANILAMIDE

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Although numerous toxic effects of sulfanilamide have been described, there are only a few references in the literature to damage to the liver produced by this drug. Hageman and Blake [1] have observed one case of toxic hepatitis presumably due to sulfanilamide. This patient recovered promptly when the drug was discontinued. Saphirstein [2] has recorded a severe but nonfatal case of toxic hepatitis caused by sulfanilamide. In this instance there was an associated exfoliative dermatitis.

Two deaths from hepatitis following the use of sulfanilamide have been reported by Bannick, Brown and Foster.[3] They felt that possibly their patients suffered hepatic damage prior to the beginning of the treatment and concluded that sulfanilamide may cause preexisting hepatic damage to progress to a stage from which regeneration is impossible. In contrast to this complication they have seen mild attacks of jaundice, which usually subsided rapidly when use of the drug was discontinued and intake of fluids was forced.

Long [4] in his experience with sulfanilamide has encountered jaundice with marked decrease of hepatic function on only one occasion. He believes that previous hepatic damage or jaundice is not necessarily a contraindication of sulfanilamide therapy.

This communication reports five cases of toxic hepatitis apparently caused by sulfanilamide, and increases the evidence that this drug is capable of causing severe damage to the liver.

CASE 1.—N. M., a white man, aged 25, who entered the Cleveland City Hospital Nov. 6, 1937, complained of a cutaneous disorder.

October 16 he had been started on a course of sulfanilamide as treatment for gonorrheal prostatitis. No other medication was administered. October 29 the patient had a chill followed by a fever of 38.5 C. (101.3 F.). The sulfanilamide was discontinued at once, a total of 50 Gm. having been given. November 4 a generalized cutaneous eruption appeared, and the patient became acutely ill. He entered the hospital two days later.

Examination showed the cutaneous eruption to consist of confluent red maculopapules with a few minute vesicles and pustules. General examination was otherwise negative except that the temperature was 38 C. (100.4 F.) and the liver and spleen were just palpable. Within the next few days the cutaneous eruption became more severe and icterus appeared. The edge of the liver was now 5 cm. below the costal margin.

From the Department of Medicine of Cleveland City Hospital and the Western Reserve University School of Medicine.

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3. Bannick, E. G.; Brown, A. E., and Foster, F. P.: Therapeutic Effectiveness and Toxicity of Sulfanilamide and Several Related Compounds, J. A. M. A. **111**: 770-777 (Aug. 27) 1938.
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On the third hospital day, the urine contained both bile and urobilinogen, and the icteric index was 63. On the sixth hospital day examination of the blood revealed sulfanilamide 0.2 mg. per hundred cubic centimeters, urea nitrogen 13 mg., sugar 83 mg., cholesterol 232 mg. and phosphatase 15.6 mg. The leukocytes numbered 19,000 per cubic millimeter and the erythrocytes 4,200,000. The hemoglobin was 12.1 Gm. per hundred cubic centimeters and a smear of the blood was normal. The Kline test for syphilis was negative.

During the next week the patient became deeply jaundiced, stuporous and very ill. The temperature varied between 38 and 40 C. (100.4 and 104 F.), the respiratory rate between 30 and 40 per minute and the pulse rate between 100 and 130 beats per minute. The cutaneous eruption progressed into a typical exfoliative dermatitis. The edge of the liver was now 10 cm. below the costal margin and the abdomen was distended with fluid. The urine contained large amounts of bile and urobilinogen, and the stools were light in color.

The therapy during this period consisted of a high carbohydrate-low fat diet, insulin, intravenous dextrose, blood transfusion, forced fluids, emollients and symptomatic treatment. On the thirteenth hospital day the patient began to improve. The temperature returned to normal. The fluid in the abdomen absorbed rather rapidly. The icterus slowly decreased, as did the bile and urobilinogen in the urine. The skin and the liver gradually returned to normal, and the patient was discharged on the thirty-eighth hospital day.

CASE 2.—G. B., a Negro woman aged 24, who entered the Cleveland City Hospital April 5, 1938, had received 33 Gm. of sulfanilamide from February 28 to March 10 inclusive for an infection of the pelvis. The patient then changed physicians and on March 16 received a single 0.6 Gm. dose of sulfanilamide, which caused her to have fever. Again on March 26 she received another 0.6 Gm. dose of sulfanilamide. No other medication was given. Following the last dose of sulfanilamide the patient's temperature varied between 38.5 and 39 C. (101.3 and 102.2 F.). March 30 she became icteric and the urine contained bile. The following day a generalized dermatitis appeared and thereafter the patient became acutely ill, entering the hospital five days later.

Examination showed a generalized exfoliative dermatitis and moderate jaundice. The edge of the liver was palpable 10 cm. below the costal margin. There was moderate thickening of both fallopian tubes. The urine contained bile grade 4 plus and urobilinogen grade 2 plus. The icteric index was 69. The erythrocytes numbered 2,500,000 per cubic millimeter, the leukocytes 30,000 and the value of the hemoglobin was 50 per cent. A differential count showed the leukocytes to be 50 per cent lymphocytes. The Kline test for syphilis was negative.

Therapy consisted of forcing fluids, high carbohydrate-low fat diet, intramuscular liver, ferrous carbonate by mouth, insulin, intravenous dextrose, blood transfusion and symptomatic treatment, but the patient became progressively worse and died April 10, on the fifth hospital day. Permission for a postmortem examination was not obtained.

CASE 3.—G. D., a white man aged 41, entered the Cleveland City Hospital Dec. 14, 1937, because of erysipelas of two days' duration. The patient said that he had drunk about 1 quart (liter) of whisky daily for the past fifteen years, although he had not taken any for a few days prior to his admission to the hospital.

Except for the erysipelas, the general physical examination was negative and sulfanilamide therapy was begun. No whisky or other medication was administered. On the third hospital day it was noted that the edge of the liver was 2 cm. below the costal margin. The sulfanilamide accordingly was discontinued at once, the patient having received a total of 26 Gm. The blood sulfanilamide was 15 mg. per hundred cubic centimeters. On the sixth hospital day the edge of the liver extended 6 cm. below the costal margin. The patient was jaundiced and the urine contained bile grade 4 plus. The stools were not acholic and the spleen could not be palpated. At this point the patient started to improve. The erysipelas and jaundice cleared rapidly and the liver decreased in size, the patient being discharged on the fifteenth hospital day.

Repeated blood studies showed no abnormalities except for leukocytosis at the time the erysipelas was present. The Kline test for syphilis was negative.

CASE 4.—T. J., a white man aged 40, who entered the Cleveland City Hospital Oct. 4, 1937, had received 35 Gm. of sulfanilamide from September 17 to October 3 inclusive because of chronic prostatitis. No other medication was administered. Two days before the sulfanilamide was discontinued the patient noted jaundice and vague epigastric pain.

General physical examination was negative except that the skin was moderately icteric and the liver extended 3 cm. below the costal margin. The urine contained large amounts of bile. Examination of the blood revealed the icteric index 63, phosphatase 18.1, phosphorus 2.6 mg. per hundred cubic centimeters, cholesterol 142 mg., sugar 83 mg., urea nitrogen 13 mg. The Kline test for syphilis was negative.

The jaundice gradually increased until the ninth hospital day, when the icteric index was 160. At this time the edge of the liver was 8 cm. below the costal margin. Thereafter the icterus slowly decreased and the liver returned to normal size, the patient being discharged November 9 in good health on the thirty-sixth hospital day. He was not seriously ill at any time nor did any anemia appear. Cholecystograms taken November 19 (ten days after discharge) were negative.

CASE 5.—T. M., a Negro aged 28, entered the Cleveland City Hospital Aug. 4, 1937, because of second degree burns of the left hand and left leg. In order to combat secondary infection, 44 Gm. of sulfanilamide was given from August 12 to August 22 inclusive without effect. The drug was again given from October 14 to October 17 inclusive, 16 Gm. being administered. The other medications given during this period were tannic acid, silver nitrate, boric acid ointment, potassium permanganate and dilute solution of sodium hypochlorite locally, and morphine, codeine, phenobarbital, acetophenetidin, acetylsalicylic acid and chloral derivatives. The Kline test for syphilis was negative.

November 30 a generalized erythematous maculopapular eruption appeared. Within the next week this progressed into an exfoliative dermatitis. The patient also became icteric and the edge of the liver, previously not palpable, was now 6 cm. below the costal margin. The icteric index rose rapidly to 115 and large amounts of bile appeared in the urine. There was no concomitant anemia. December 22 the skin started to improve and returned to normal rather rapidly. The icterus decreased slowly, as did the size of the liver. Feb. 4, 1938, when he was discharged, the icteric index was 20, the liver was no longer palpable and the patient felt normal.

COMMENT

In case 1 there is no reasonable doubt that sulfanilamide caused the dermatitis and hepatitis. No other medication was administered, and the cutaneous eruption was a typical dermatitis medicamentosa, the hepatic disease a typical toxic hepatitis.

The case is extraordinary in that there was simultaneous occurrence of jaundice and ascites with recovery. The first description of a case of jaundice and ascites with recovery is accredited to Jones and Minot[5] in 1923. Subsequently similar observations have been made by Bauer,[6] Weir,[7] Meyer and Learner,[8] McCabe and Hart,[9] Cavanagh,[10] Pavel and Runcan,[11] Forbes[12]

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7. Weir, J. F.: Association of Jaundice and Ascites in Diseases of the Liver, J. A. M. A. **91**: 1888-1891 (Dec. 15) 1928.
8. Meyer, Jacob, and Learner, Aaron: Ascites Occurring During Jaundice with Recovery, J. A. M. A. **104**: 114-116 (Jan. 12) 1935.
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10. Cavanagh, J. R.: Jaundice and Ascites with Recovery: Case Report, M. Ann. District of Columbia **4**: 322-324 (Dec.) 1935.
11. Pavel, I., and Runcan, I.: Difficulties of Pathogenic Diagnosis; Unusual Case History of Jaundice and Ascites, Paris méd. **1**: 432-434 (May 16) 1936.
12. Forbes, J. R.: Case with Ascites Due to Novarsobenzol (Neoarsphenamine), Guy's Hosp. Rep. **85**: 161-162 (April) 1935.

and Boros.[13] These reports have indicated that arsphenamine, mercurial products, phosphorus, sodium gold thiosulfate, cinchophen, common duct stone, pressure of glands on the common duct and infections are agents which can so damage the parenchyma of the liver as to produce both jaundice and ascites and yet permit recovery. Evidently sulfanilamide can be added to this list.

In case 2 there seems to be little doubt that the dermatitis and hepatitis were caused by sulfanilamide. No other medication had been administered and the dermatitis and hepatitis in general resembled those in case 1. Either the patient had a chronic secondary anemia or the drug was hemolytic to erythrocytes. However, the size of the liver and the degree of icterus would indicate that an acute inflammatory process was present in any event and that the jaundice was not a manifestation of hemolytic anemia. Death in this case cannot be ascribed to the hepatitis alone in view of the fact that exfoliative dermatitis and anemia were also present.

Case 3 illustrates a less severe degree of hepatitis, occurring in this instance in a patient addicted to alcohol. No medication other than sulfanilamide was administered. Whether previous ingestion of alcohol renders the liver more vulnerable to sulfanilamide cannot be stated, although numerous other patients who have used alcohol to excess have tolerated the drug satisfactorily.

Case 4 reports a typical case of toxic hepatitis of moderate severity. No etiologic agent other than sulfanilamide can be incriminated. In this case, as in case 3, there were no other toxic manifestations.

The hepatitis in case 5 cannot be ascribed to sulfanilamide with as much certainty as in the other cases. In this instance there had been an interval of forty-three days between the last dose of sulfanilamide and the onset of symptoms. However, during this period no drug ordinarily considered as capable of causing toxic hepatitis and dermatitis had been administered. Furthermore, in the case of other hepatic irritants the length of time intervening between the actual administration of the drug and the onset of symptoms has been found to be quite variable, occasionally being as much as several months.[14] Whether this will hold true for sulfanilamide as it has in the case of other drugs remains to be seen. Certain it is that the hepatitis and dermatitis in this case were virtually indistinguishable from those in case 1 and case 2.

SUMMARY

Four cases of toxic hepatitis occurred during the course of sulfanilamide therapy. No other medication had been given to these patients. A fifth case developed after the use of sulfanilamide had been discontinued. In this instance the patient had received other medications but none ordinarily considered as capable of causing toxic hepatitis.

Three of these cases of toxic hepatitis showed an associated exfoliative dermatitis and one ended fatally. One case was extraordinary in that there was a simultaneous occurrence of jaundice and ascites with recovery.

This experience indicates that sulfanilamide should be added to the list of agents which may cause severe damage to the liver.

3395 Scranton Road.

13. Boros, Edwin: Hay Fever and Asthma During and After Jaundice: Ascites Due to Cinchophen Poisoning, J. A. M. A. **109**: 113-115 (July 10) 1937.

14. Willcox, William: Toxic Jaundice, Lancet **2**: 1 (July 4) 1931.

RADIOACTIVE IRON AND ITS METABOLISM IN ANEMIA

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During the past eight months radioactive iron has been used in these laboratories as a tool in the studies of iron metabolism in dogs. This radioactive iron is prepared from the Fe^{58} isotope by deuteron bombardment

$$Fe^{58} + D^2_1 \rightarrow Fe^{59} + p$$

Its beta ray activity with a half life of forty-seven days makes this isotope useful as a labeled iron that may be followed in metabolism experiments even after mixture with the ordinary iron in the body.

Physiologists will admit that our understanding of iron metabolism is in a parlous state. There are diametrically opposed views relating to almost every phase of iron metabolism in the body. It is fair to state that much of this difficulty relates to methods of iron analysis. Many methods for iron analysis in body tissues, fluids or feces carry errors so large as to render the results useless. These errors are due in part to various compounds of calcium and phosphorus.

Radioactive Iron Content of Tissues and Blood: Percentage of Total Amount Fed

	Anemic					Normal		
Dog.....	H-9	H-8	37-116	37-227		37-77	37-144	37-214
Hours after last feeding*.....	20	23	23	4	75	84	23	7
Liver.....	0.4	0.4	0.5	..	..	0.2	0.03	0.02
Spleen.....	0	0	0.1	..	..	0	0.02	0.005
Marrow.....	0.2±	3±	2±	..	..	0	0.03±	....
Plasma.....	0	0.3	0.11	0.7	0	0	0.01?	....
Red blood cells.	8.7	9.0	1.4	0.9	4.6	0.04	0.06	....
Whole blood....	(8.7)	(9.3)	(1.5)	(1.6)	(4.6)	(0.04)	(0.07)	0.05
Total absorbed	9.3	12.7	4.1			0.24	0.15	0.08

* Dogs 37-227 and 37-214 were fed iron as ferric chloride; all others as ferric sulfate.

If one may state (with allowance for varied opinions) the generally accepted story of the absorption and excretion of iron, it would read as follows: Iron is absorbed from the upper part of the intestinal tract in amounts depending on its concentration in the food, its form (ferrous or ferric) and gastric acidity; the surplus related to iron absorption, utilization and wastage is excreted in the lower bowel.

It came as a great surprise to us that iron is absorbed only in traces by a nonanemic dog but in abundance by the anemic dog depleted of its iron. This point is clear from a review of the accompanying table, but we are not prepared to say on what factors this difference rests —whether changes in mucosa, plasma or concentration of organic iron are of primary importance.

Five dogs were maintained on a diet low in iron and kept anemic by frequent bleeding. This has been shown to affect the depletion of iron stores. They were then fed iron containing the radioactive isotope on one or several occasions and the absorption of iron was followed by analysis of the circulating blood fractions. In three experiments the dogs were killed with ether after careful viviperfusion to remove all the circulating blood

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from the viscera. The value and limitations of this technical procedure have been discussed.[1] The content of radioactive iron in the liver, spleen and marrow was then determined, as shown in the table.

In another series of experiments, radioactive iron was fed to three normal dogs with iron stores well filled as the result of previous feeding of soluble iron salts and intravenous injections of neutral colloidal iron.

It is immediately apparent, even in this short series, that the nonanemic animal absorbs but little of the iron fed. Some of the anemic animals were not perfused in order that studies of excretion over long periods of time might be made, so we have no values for the iron content of the viscera. However, the rapid appearance of the isotope in the plasma and red blood cells alone is in marked contrast to the evidence in all the viscera and blood of the normal animals examined. The rapid appearance of radioactive iron in the red blood cells is of great interest. A discussion of the significance of these observations must await further experiments to indicate the relationship of this iron to the hemoglobin of the various types of red blood cells (nucleated, immatui and mature).

CONCLUSION

The evidence appears convincing that, in dogs under the conditions of these experiments, absorption of iron is dependent on the need of the body for iron.

260 Crittenden Boulevard.

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From the National Institute of Health.

A REACTION TO THE ORAL ADMINISTRATION OF NICOTINIC ACID

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Amost all the reports on the treatment of pellagra with nicotinic acid refer to unpleasant, but harmless, reactions. Fouts, Helmer, Lepkovsky and Jukes[1] treated three cases of pellagra with 500 mg. and one case with 1 Gm. of nicotinic acid. A sensation of heat and tingling on the skin was noted in all four cases. These sensations appeared within ten minutes, lasted from ten to twenty minutes, and were accompanied by dilatation of the peripheral blood vessels and slight, temporary fall in blood pressure.

The Smiths and Ruffin[2] observed a marked flushing of the face, neck, chest and arms a few minutes after intramuscular injection of 60 mg. of nicotinic acid, which lasted for fifteen minutes. A similar reaction followed the intravenous administration of approximately 12 mg. They note that the pulse, respiration and blood pressure were not affected and that there was no discomfort except for a slight feeling of warmth.

Spies, Cooper and Blankenhorn[3] noted severe flushing, itching and tingling, particularly of the face and extremities, within twenty minutes after the administration of nicotinic acid in nine of thirteen persons. At the peak of the flushing there was no effect on blood pressure, temperature or respiration, and they state that in no instance did the administration of less than 50 mg. produce any effect, the reaction usually occurring only when large amounts were given.

France, Bates, Barker and Matthews[4] report mild generalized sensations of tingling and flushing in a case of pellagra a few minutes after the intramuscular injection of 60 mg. of nicotinic acid.

Spies, Bean and Stone[5] found that oral doses of 200 mg. of nicotinic acid or intravenous doses of 10 mg. nearly always produce a reaction within one minute. They noted reactions in about 5 per cent of 100 adults with an oral dose of 50 mg. and in about 50 per cent when 100 mg. was given. The reaction was characterized by flushing, burning and itching sensations with increased temperature of the skin and increased gastrointestinal motility. The pulse, blood pressure, respiration and electrocardiograms were not regularly changed.

Ruffin[6] states that 1 Gm. daily given in four doses invariably produces unpleasant sensations and flushing of the face and neck. In two of ten cases nausea and vomiting occurred.

Bogart[7] gave one patient 500 mg. daily until 8 Gm. was given and 300 mg. daily until 6 Gm. was given, and noted redness and warmth of the skin on only two occasions.

Rachmilewitz and Glueck[8] report one case of pellagra with tingling of finger tips, flushing of face and dizziness following 250 mg. of nicotinic acid for one day and 350 mg. daily for four days. In a second case severe itching occurred over the dermatitis, with flushing of the face, faintness and urticarial rash over the knees, back and arms following a second dose of 50 mg.

In view of these reports it seemed desirable to determine the quantity of nicotinic acid which may be given by mouth to healthy subjects without producing these unpleasant reactions which tend to make continued treatment with the drug more difficult. Accordingly, a group of eighteen healthy adult women were given an identical diet containing approximately 2,400 calories and low in the pellagra-preventive vitamin. Six were given 50 mg., six 30 mg. and six 10 mg. of nicotinic acid daily in aqueous solution added to 4 ounces (120 cc.) of tomato juice and taken with the midday meal. On the twelfth day of administration one of the subjects receiving 50 mg. daily (total intake of nicotinic acid 600 mg.) showed an intense flushing of the face, chest and back, accompanied by mild itching and a sensation of heat in the skin, which appeared in from ten to fifteen minutes after administration of the nicotinic acid and disappeared after about an hour. Following this first reaction, each daily dose of 50 mg. produced a similar reaction for eleven days. The dose was then divided into 25 mg. morning and evening. The flushing became much less marked and the subjective symptoms were milder but still occurred.

1. Fouts, P. J.; Helmer, O. M.; Lepkovsky, Samuel, and Jukes, T. H.: Treatment of Human Pellagra with Nicotinic Acid, Proc. Soc. Exper. Biol. & Med. **37**: 405 (Nov.) 1937.
2. Smith, D. T.; Ruffin, J. M., and Smith, Susan G.: Pellagra Successfully Treated with Nicotinic Acid, J. A. M. A. **109**: 2054 (Dec. 18) 1937.
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5. Spies, T. D.; Bean, W. B., and Stone, R. E.: The Treatment of Subclinical and Classic Pellagra: Use of Nicotinic Acid, Nicotinic Acid Amide and Sodium Nicotinate, with Special Reference to the Vasodilator Action and the Effect of Mental Symptoms, J. A. M. A. **111**: 584 (Aug. 13) 1938.
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7. Bogart, C. N.: Nicotinic Acid in the Treatment of Pellagra, J. A. M. A. **111**: 613 (Aug. 13) 1938.
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On the sixteenth day of administration a second subject receiving 50 mg. daily (total intake of nicotinic acid 800 mg.) showed a similar reaction of severe flushing of the face.

On the twenty-seventh day two more of the group receiving 50 mg. of nicotinic acid daily (total intake of nicotinic acid 1,350 mg.) showed similar reactions of slight flushing, itching and a sensation of heat. The remaining two subjects of this group did not show any reaction during a period of ninety-two days on the 50 mg. of nicotinic acid daily.

One of the six subjects receiving 30 mg. of nicotinic acid daily had a reaction on the thirty-second day (total nicotinic acid 660 mg.), characterized by an intense flushing of the face and neck, with itching and a sensation of heat. When the dose was continued the reaction occurred occasionally.

On the ninety-second day a second subject receiving 30 mg. daily (total intake of nicotinic acid 2.76 Gm.) had a similar reaction, which was unusual in that the flushing was restricted to the skin of the forehead, bridge of the nose, cheeks, back of the neck, shoulder joints, elbows, buttocks and knees. The remaining four subjects in the group did not show any reaction during the period of ninety-two days on the 30 mg. of nicotinic acid daily. None of the six subjects receiving the 10 mg. dose of nicotinic acid had a reaction at any time during the ninety-two days of observation.

The four subjects in the 50 mg. group who had reactions weighed 128, 101, 140 and 108 pounds (58, 46, 63.5 and 49 Kg.). The two who had no reactions weighed 165 and 111 pounds (75 and 50 Kg.). The two subjects in the 30 mg. group who had reactions weighed 119 and 113 pounds (54 and 51 Kg.). The remaining four weighed 147, 132, 99 and 143 pounds (67, 60, 45 and 65 Kg.). Thus there appears to be a considerable individual variation in reactions to nicotinic acid given by mouth which does not depend on the relationship between dosage and body weight, although this cannot be stated with certainty since the degree of saturation of the subjects with nicotinic acid at the beginning of the test is unknown.

In view of the fact that the reactions did not recur regularly in any of the patients except one in the 50 mg. group, and since Spies, Bean and Stone [5] report reactions within one minute from the intravenous injection of 10 mg., and the Smiths and Ruffin [2] report reactions from 12 mg. intravenously, it is not unlikely that one of the controlling factors in this reaction to the oral administration of nicotinic acid is the rate of absorption from the gastrointestinal tract.

CONCLUSIONS

Nicotinic acid in daily doses of 50 mg., given orally, produced transient, unpleasant but harmless reactions in four of six adult women on a diet restricted in the pellagra-preventive factor. A daily dose of 30 mg. of nicotinic acid produced a similar reaction in two of six women. Therefore reactions are to be expected in some persons on continued treatment with nicotinic acid in daily doses as low as 30 mg. by mouth.

Although the reactions are disagreeable, they persist only a short while and there is no evidence that any harm is done by them. Therefore their occurrence should not be allowed to interfere with the therapeutic use of large doses of nicotinic acid.

THE PRIVATE PHYSICIAN'S ROLE IN THE NEW YORK CITY SYPHILIS CONTROL ACTIVITIES

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Not merely in words but also in action the New York City Department of Health has expressed its belief that the role of the private physician in the control of syphilis and gonorrhea is of paramount importance. There are about 15,000 private physicians in this city. They are in every neighborhood, available to aid diseased persons with advice, diagnosis and treatment. A large percentage of them welcome the opportunity to give medical care to persons having syphilis or gonorrhea and they welcome that official aid which enables them to render these services to a larger and larger number of victims of infection. They are willing to learn modern methods of diagnosis and treatment if they are not already familiar with them. They are willing to use modern diagnostic facilities, to seek consultation, to accept appropriate drugs, to report their cases, to cooperate in finding sources of infection, to notify the department of health regarding lapsed cases and to aid in popular education of the general public regarding syphilis and gonorrhea. They benefit and the official health agency benefits by this cooperation.

The health department should study seriously and frequently the question What can we do to help private physicians find, treat and keep under treatment more and more persons with gonorrhea and syphilis, especially those who can pay a fee, even though a very modest one? No health department can afford to neglect measures for obtaining the cooperation of private physicians. If the cooperation of the official agency is sincere—with emphasis on the "co"—and not merely a onesided demand for reports and red tape performances from private physicians, the results will be satisfactory to all concerned.

Coöperation with private physicians was the basis of the policy of the New York City Department of Health when in October 1935 Commissioner John L. Rice created a Bureau of Social Hygiene to develop a program for the control of syphilis and gonorrhea in our population of seven and a half million people. Administrative details have been carefully considered with the medical advisory committees of the department and of the several health districts of the city.

As a preliminary step in this process of cooperation with private physicians a twofold plan of disseminating popular and professional information was set up. In order to meet the needs of practitioners who were not thoroughly familiar with modern methods of diagnosis and treatment of syphilis and gonorrhea, four postgraduate clinical courses, each of six weeks' duration and requiring attendance three times weekly, were given in succession in 1937. Registration was limited to ten physicians for each of these sessions, which included lectures and clinical demonstration. During the spring of 1938 a "refresher course" was held once a week for six weeks; the attendance throughout was maintained at seventy doctors for each meeting. In fact, this course was so well received that it was

decided to hold a similar series during the summer months. In spite of the seasonal inactivity, an average of forty physicians attended each session. Local and national medical groups holding periodic meetings in New York City include in their programs sections on control of syphilis and gonorrhea. For example, during the week of the annual meeting of the American College of Physicians, one section met daily at the

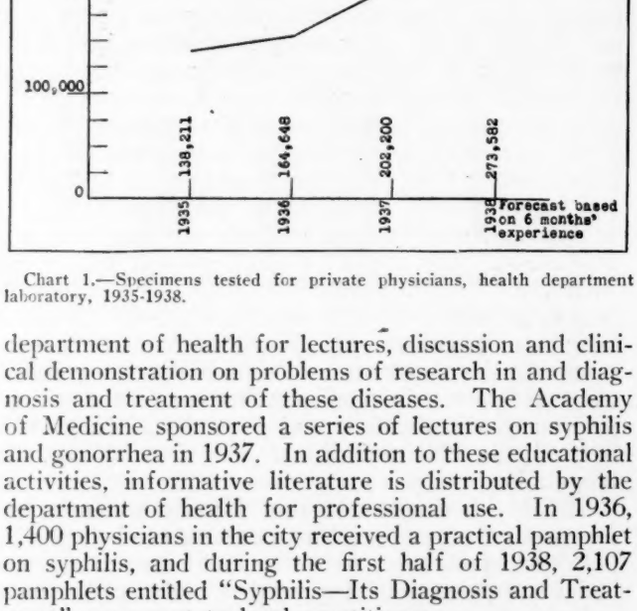

Chart 1.—Specimens tested for private physicians, health department laboratory, 1935-1938.

department of health for lectures, discussion and clinical demonstration on problems of research in and diagnosis and treatment of these diseases. The Academy of Medicine sponsored a series of lectures on syphilis and gonorrhea in 1937. In addition to these educational activities, informative literature is distributed by the department of health for professional use. In 1936, 1,400 physicians in the city received a practical pamphlet on syphilis, and during the first half of 1938, 2,107 pamphlets entitled "Syphilis—Its Diagnosis and Treatment" were sent to local practitioners.

Private practitioners have in turn united with the health department in enlightening the general public. During the 1937-1938 season, forty-five doctors, not connected with the department in any way, gave eighty-one lectures, accompanied by film showings, to general

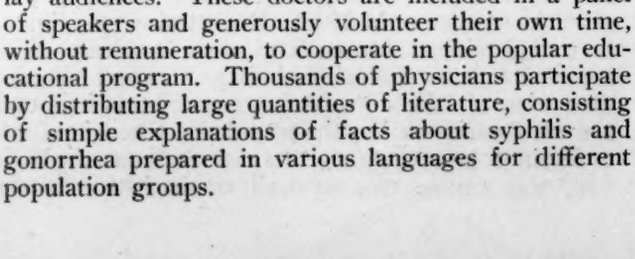

Chart 2.—Number of private physicians receiving drugs, October 1936 to June 1938.

lay audiences. These doctors are included in a panel of speakers and generously volunteer their own time, without remuneration, to cooperate in the popular educational program. Thousands of physicians participate by distributing large quantities of literature, consisting of simple explanations of facts about syphilis and gonorrhea prepared in various languages for different population groups.

All educational propaganda issue by the department of health stresses the desirability of undergoing examination and treatment, if necessary, by the family physician. Every possible aid is extended to the doctor in carrying out this objective. Among diagnostic services offered the physician is free laboratory service, including blood, dark field and spinal fluid examinations for syphilis and smear tests for gonorrhea. One-half million such tests are performed annually in the health department laboratories, and of these more than 50 per cent are sent in by private physicians. That this service is constantly increasing is evident by chart 1.

Private physicians may send their patients to any one of twenty centers for diagnostic and consultation services; the results of such examinations, which vary from the taking of a specimen to performing a complete examination for a venereal disease, are sent directly to the physician referring the patient. Table 1 indicates the number of laboratory specimens taken in health department clinics on patients referred by private physicians; it will be noted that an increase of 20 per cent over the number examined in 1937 is expected in this service during 1938.

The department of health has repeatedly announced that persons wishing to place themselves under the care of private physicians can obtain the names of private physicians from the diagnostic and treatment centers of

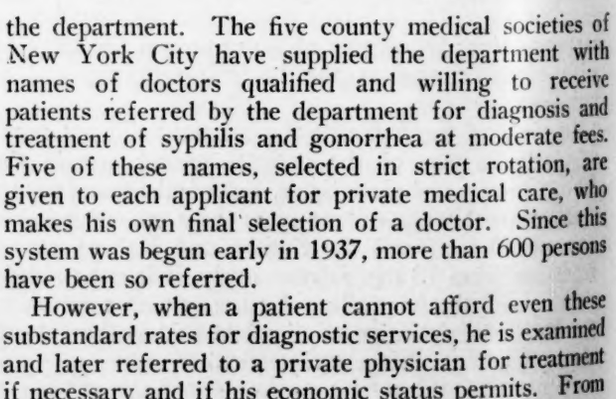

Chart 3.—Private physicians visited by epidemiologists, 1937-1938.

the department. The five county medical societies of New York City have supplied the department with names of doctors qualified and willing to receive patients referred by the department for diagnosis and treatment of syphilis and gonorrhea at moderate fees. Five of these names, selected in strict rotation, are given to each applicant for private medical care, who makes his own final selection of a doctor. Since this system was begun early in 1937, more than 600 persons have been so referred.

However, when a patient cannot afford even these substandard rates for diagnostic services, he is examined and later referred to a private physician for treatment if necessary and if his economic status permits. From 200 to 300 persons annually are referred to private physicians for treatment subsequent to examination in health department clinics. A reciprocal relationship allows the private doctor to send his patients to the health department for treatment if he finds such an arrangement desirable; more than 1,000 patients are referred by private physicians each year for treatment by the department of health.

One of the most important items in placing and keeping patients under the care of private physicians is the practice of the distribution of free drugs for the treatment of syphilis. From August 1936, when distribution began, through June 1938, a period of twenty-two months, 420,448 doses of drugs were given

to private practitioners for the treatment of their private patients, regardless of their economic status and in sufficient amounts to give thorough and complete treatment. More than 600 doctors a month receive drugs for the treatment of almost 1,000 patients. Chart 2 indicates the extent to which this practice is expanding.

The problems of helping physicians to find new patients with syphilis and gonorrhea and keep them under their care have been satisfactorily solved by the methods briefly outlined. However, the necessity for extending these services to provide for the investigation of contacts, sources of infection and the follow-up of delinquent cases was met by employing, in December 1936, a staff of four medical epidemiologists and eight nurse epidemiologists. Any physician is at liberty to request the assistance of a member of this group, who, for the duration of his relationship with the physician, serves under the latter's supervision.

Medical epidemiologists, on request, frequently confer with doctors regarding their problems of diagnosis and treatment and help them bring in for examination possible sources of infection and contact to their patients. Chart 3 indicates the number of visits made to private physicians by epidemiologists, at the physicians' request.

During 1937, 433 named possible sources of infection were referred by doctors for investigation, of whom

TABLE 1.—*Specimens Taken for Private Physicians at Social Hygiene Clinics for Wassermann, Dark Field and Smear Examinations in New York City, 1935-1938*

1935	1936	1937	Forecast for 1938*
13,006	11,554	12,815	15,172

* Based on six months' experience.

TABLE 2.—*Reported Cases of Syphilis and Gonorrhea in New York City During First and Second Quarter of 1938*

Reporting Agency	First Quarter	Second Quarter	Percentage Increase
Health Department Clinics	1,506	3,542	135
Nondepartment clinics	4,149	5,489	32
Private physicians	2,593	5,857	126
Other	35	1	−97
Totals	8,283	14,889	80

134, or 31 per cent, were subsequently proved sources of infection. They also referred 217 contacts to their patients, of whom 204, or 94 per cent, were brought in for examination. Thus, it is obvious that one of the major obligations of the medical epidemiologist is serving the private practitioner in any capacity relevant to the control of syphilis and gonorrhea.

Nurse epidemiologists follow up patients reported as delinquent by private physicians; in their dealings with these patients they act as agents of the doctors. Their chief concern is the return of the patient to the referring physician; if such action is impossible, the nurse makes an effort to place him under other medical supervision. During the second quarter of 1938 a brief study was made of the results of following up and tracing delinquent patients reported by private practitioners. In this period 360 new referrals were made, of which 270 were terminated. Of these 270 terminations, 103 were not found because the patient had given the physician a false address or because the patient had left the city. Thus 167 of these persons were located, of whom 50 per cent were returned to private physicians. Most doctors are not able to follow up their own delinquent patients and find it very convenient to enlist the help of a nurse epidemiologist. As more doctors become familiar with this service, more of the nurses' time is devoted to their patients. Chart 4 shows the ratio of private physicians' cases to the total number of lapsed cases referred for follow up since the beginning of 1937, when this item in the control program was introduced.

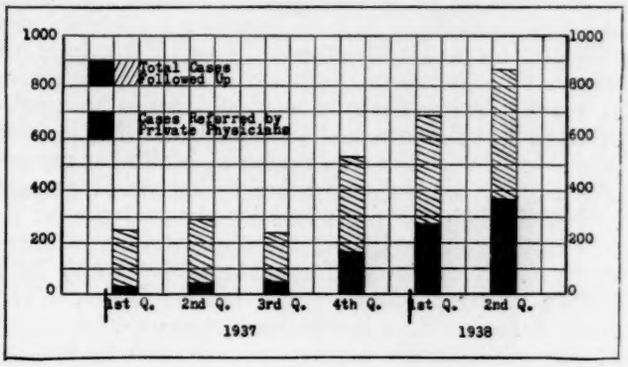

Chart 4.—Cases referred by private physicians for follow up by nurse epidemiologists.

Case reporting by private physicians has improved to the extent at which it is now possible to omit positive laboratory reports from the official case count. Every physician who submits to the health department laboratories a positive blood or smear specimen is sent a letter requesting him to report the patient if a diagnosis of syphilis or gonorrhea is made and if the report had not previously been made. These individual letters

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1. Laboratory Examination:
   (*a*) Dark field for Spirochaeta pallida.
   (*b*) Smears for gonococci and Ducrey bacilli.
   (*c*) Blood Wassermann tests.
   (*d*) Spinal fluid examination for neurosyphilis.
   (*e*) Frei tests for lymphogranuloma venereum.
2. Lumbar Puncture.
3. Clinical Consultation Service (Diagnosis and Treatment). Reports mailed only to referring physician.
4. Antisyphilitic drugs: Neoarsphenamine and bismuth compounds distributed free of charge.
5. Epidemiologic Service:
   As representative of referring physician.
   (*a*) Investigation of sources of infection on request and only with consent of physician.
   (*b*) Follow up of family and other contacts and cases lapsing treatment.
6. Postgraduate instruction in the diagnosis and management of syphilis.
7. Clinical conferences at the Bureau of Social Hygiene.
8. Posters and literature for patients.
9. Listing through local county medical society qualified physicians willing to treat referred patients at moderate fees.

Preserve This Card for Future Reference

Announcement sent by laboratory with reports on specimens.

are not only directly responsible for the great improvement in case reporting but have also proved to be a valuable means for bringing to the attention of the department delinquency in treatment. This system was instituted during the first quarter of 1938 and has begun to produce excellent results. During the first three months of the year 8,281 cases of syphilis and gonor-

rhea were reported as compared with 14,889 for the second quarter, an increase of 80 per cent. It is particularly interesting to note that private physicians have improved their official case reporting during that time by 126 per cent and now constitute the largest reporting agency, as indicated in table 2.

The greatest problem still remaining in this program of coordinating the activities of the medical and public health professions is that of acquainting more doctors with the services offered them. In their efforts to inform their members of health department activities in this connection, the local medical societies have published progress reports and occasional editorials in their official bulletins. The department of health has repeatedly circularized the profession by means of general letters, through the press and by personal contact as well as through the laboratory, which sends announcements (such as the card reproduced herewith) in a routine manner with reports on specimens. The demand for services is rapidly increasing as a result of this publicity; the department will continue to keep pace with this growing interest by emphasizing cooperation with the medical profession.

SUMMARY AND CONCLUSION

In New York City the department of health offers to private physicians postgraduate educational opportunities, all diagnostic and consultation services, epidemiologic and follow-up services, and drugs for the control of syphilis and gonorrhea. The private practitioners of the city have welcomed these services and have given their cooperation in finding and treating these diseases.

50 West Fiftieth Street.

Clinical Notes, Suggestions and New Instruments

SENSITIZATION REACTION TO SULFANILAMIDE

E. B. ROGERS, M.D., EL PASO, TEXAS

Many reports of eruptions of the skin have been described as having resulted from sulfanilamide. Dermatitis medicamentosa, a simple maculopapular rash, has appeared during the second week of treatment in about 6 per cent of cases.[1] It usually disappears in two or three days after treatment has been discontinued. Erythematous eruptions covering part or all of the body have been described [2] and there have been some cases of exfoliative dermatitis which cleared up only after several months.[3] Only one report of definite sensitization to the drug has come to my attention, in an unpublished personal communication; hence the following case report seems worthy of notice.

REPORT OF CASE

Mrs. R., aged 58, an American housewife with two children, gave a past history of allergy. In 1921, to relieve severe pruritus vulvae, a resection of the left ilio-hypogastric and ilio-inguinal nerves was done under 1 per cent procaine hydrochloride local anesthesia. Later a tooth was extracted with procaine hydrochloride as the anesthetic agent. No reaction resulted. In 1923 a sebaceous cyst was removed from the back of the neck under procaine hydrochloride. After about a week an area of redness appeared in the surrounding skin which had the appearance of an infection, but there was no pus at any time. There was much itching, which disappeared together with the redness in about three weeks. Three years later another dentist blocked a nerve with tutocain, assuring her that this was not procaine hydrochloride and would not produce a reaction. However, a severe reaction followed with redness and swelling. The gums healed slowly over a period of three or four weeks. At another time the addition of butyn to a prescription for pain in the left eye caused redness, itching and closure of the eye from swelling within twenty-four hours. The reaction was severe for a week and cleared up in three weeks. In 1930 a thoracentesis was done by one of my associates, who used procaine hydrochloride, not knowing the patient was allergic to this anesthetic. Resection of a rib was then done under gas. The area about the wound became red after a few days but the patient was too ill with empyema to note subjective symptoms.

In 1935 the patient had erysipelas originating in a small area of eczema above the right ear, which yielded to treatment with ultraviolet rays. Early in May 1938 a threatened return of the erysipelas led to sulfanilamide therapy. She took five tablets, a total of 25 grains (1.6 Gm.) in thirty-six hours. The next morning her left eye was red and the lids were greatly swollen. The conjunctiva was much congested and there was marked lacrimation. Bright red erythema covered the lids and spread over about 1 inch (2.5 cm.) of the surrounding skin. Itching of the lids was intense, especially along the margins and at the outer canthus. The right eye was normal. At the same time an area of erythema and swelling appeared in the left groin, centering over the site of the resection of the nerves, and extended gradually for a period of about two weeks. The swelling extended about 3 inches (7.6 cm.) in advance of the erythema and was marked by a sharply defined raised border similar to erysipelas, but the tissues were very soft. The temperature and pulse were normal throughout.

In the succeeding three to ten days every site of a previous application of a local anesthetic flared up in reaction—bright red erythema, itching, swelling and tenderness on pressure. The site of injection on the neck flared up on the third day, the site of injection for resection of the rib on the sixth day and the buccal mucosa about the tenth day, and later the eczematous area was found to present a red rash. The time of appearance and the intensity of reaction in all three areas seemed to depend on the quantity of anesthetic that the tissues had received at the time of operation. The eye, commonly used for sensitization tests, reacted first, and no one could fail to see that the ophthalmic reaction was strongly positive. The reaction on the groin spread over the abdomen and both thighs. The erythema in the neck and chest reached diameters of 6 and 10 inches (15 and 25 cm.). The reaction in the patch of eczema was small; it probably resulted from an external application of an anesthetic ointment. The reaction of the buccal mucosa was limited to the mucous membrane of the mouth, tongue and throat. The process in all the affected areas reached its height during the third week, at which time fully one third of the body surface was involved. Decline of the reactions then began very slowly, and at the end of five weeks there is still itching and erythema in the groin and on the back. She is not allergic to proteins, unless the eczema is of that nature.

An intolerable itching in all the affected areas was the principal symptom. Neither epinephrine nor ephedrine had any effect. The best relief was obtained from antipruritic lotions containing phenol or from the soothing effect of starch water. At one time the patient applied ethylaminobenzoate (anesthesin) ointment over a small area, which gave temporary relief but later aggravated the symptoms. Barbiturates were necessary for sleep.

The chemical formulas are given here for comparison:

Procaine hydrochloride — para-amidobenzoyl diethylaminoethanol hydrochloride.

Tutocain — para-aminobenzoyl dimethylaminomethyl-butanol hydrochloride.

Butyn—para-aminobenzoyl gamma-di normal butylaminopropanol sulfate.

Sulfanilamide—para-aminobenzene sulfonamide.

Anesthesin—ethyl aminobenzoate.

1. Schwentker, F. F., and Gelman, Sidney: Bull. Johns Hopkins Hosp. **61**: 136 (Aug.) 1937.
2. Finney, J. O: Severe Dermatitis Medicamentosa Following the Administration of Sulfanilamide, J. A. M. A. **109**: 1982 (Dec. 11) 1937.
3. Myers, G. B.; Vonder Heide, E. C., and Balcerski, Matthew: Exfoliative Dermatitis Following Sulfanilamide, J. A. M. A. **109**: 1983 (Dec. 11) 1937.

The base of each of these compounds is aminobenzene (aniline). From the injections of procaine hydrochloride the patient evidently became sensitized to compounds containing this base. If the sulfanilamide had been given by injection the result would doubtless have been the same—a flare-up reaction in areas that had previously been sensitized. Cutaneous scratch tests gave a positive wheal to 2 per cent procaine hydrochloride in twelve hours, redness in twenty-four hours, followed by itching and swelling in the subcutaneous tissues which increased gradually for a week before recession began. There was a slight reaction to aminobenzene, none to sulfanilamide. Patch tests gave negative results. Eight days after the patch tests were applied the 2 per cent procaine test gave a positive result with a papulovesicular (2 cm. in diameter) rash that faded out slowly, about two weeks later. The notable feature is that a drug taken by mouth should produce reactions at the sites of injections made years before and at no other place. This would seem to mark the process as a form of allergy but differs from food allergy in that the reaction occurs only in areas previously sensitized by some derivative of the aminobenzene base.

610 Martin Building.

STANDARDS FOR RED BLOOD CELL INCREASE AFTER LIVER AND STOMACH THERAPY IN PERNICIOUS ANEMIA

RAPHAEL ISAACS, M.D.; FRANK H. BETHELL, M.D.; MATTHEW C. RIDDLE, M.D., AND ARNOLD FRIEDMAN, ANN ARBOR, MICH.

Data from 129 selected patients with pernicious anemia in relapse, adequately treated with liver extract intramuscularly, and twenty-one patients treated with desiccated, defatted stomach tissue have been analyzed to note the rate of increase in the red blood cell count. The dosage of liver extract averaged the equivalent of from 1 to 2 units daily, and the desiccated stomach dosage was usually 40 Gm. daily for the first two weeks.

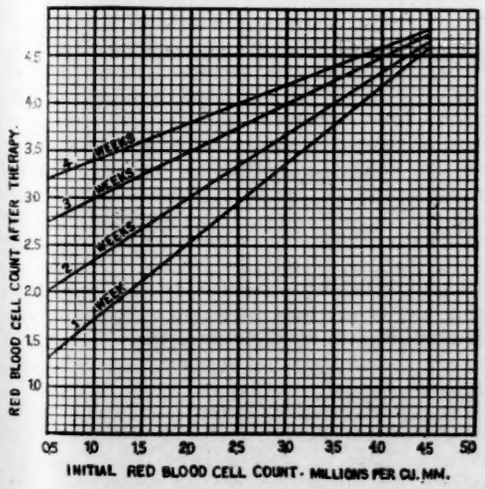

Chart 1.—The red blood cell count after one, two, three and four weeks of intramuscular liver extract therapy. Example: With an initial red blood cell count of 2 million per cubic millimeter the count at the end of one week will be 2.55 million, at two weeks 3 million, at three weeks 3.5 million, at four weeks 3.8 million.

In chart 1 the red blood cell count at the beginning of intramuscular liver extract therapy is plotted against the red blood cell count at the end of one, two, three and four weeks. A separate line is drawn for each week. The lines have been smoothed and corrections have been made for deviations due to manifest abnormalities and inadequate data at various points, as indicated by evident interpolations. Data from more than 500 cases were available for such changes.

In chart 2 the same data are plotted, showing the average rate of formation of red blood cells after intramuscular liver extract therapy, in terms of weekly changes for each initial count. From the trend of these lines, checked by available data, the positions for five, six, seven and eight weeks are indicated. If the rate remains unchanged a count of five million red blood cells per cubic millimeter may be expected at the end of eight weeks, regardless of the initial count. Many factors may modify this in individual cases, such as infection, deficiency of iron and an abnormal rate of blood destruction.

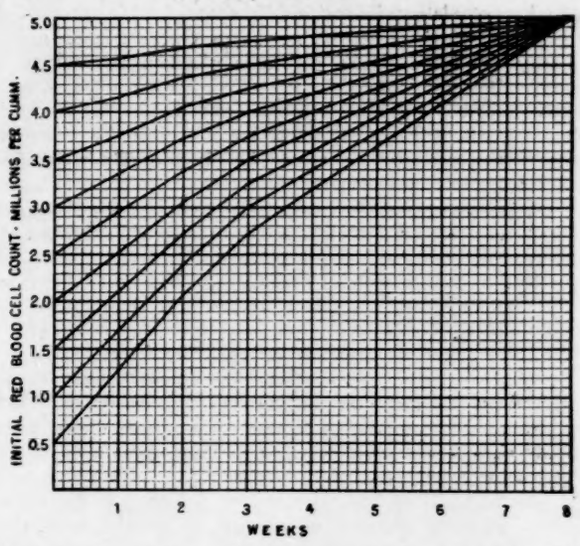

Chart 2.—The red blood cell count, at weekly intervals, for each initial red blood cell count after liver extract therapy, intramuscularly. Example: With an initial red blood cell count of 1 million per cubic millimeter the count at the end of one week will be 1.7 million, at two weeks 2.4 million, at fifteen days 2.5 million, and so on.

The rate of increase of red blood cells is slower during the first two weeks after desiccated defatted stomach tissue is given than after intramuscular liver extract (chart 3). An analysis of these data, if plotted with "weeks" as ordinates and the "initial red blood cell count" as abscissas, shows that the rise in the red blood cell count, after stomach medication, is very slight during the first week, contrasting with the more rapid increase after intramuscular liver extract medication. It is possible that this is related to the speed of absorption of the material by the intramuscular route. The slope of the line shows that the rise would begin on the fourth day of treatment with stomach.

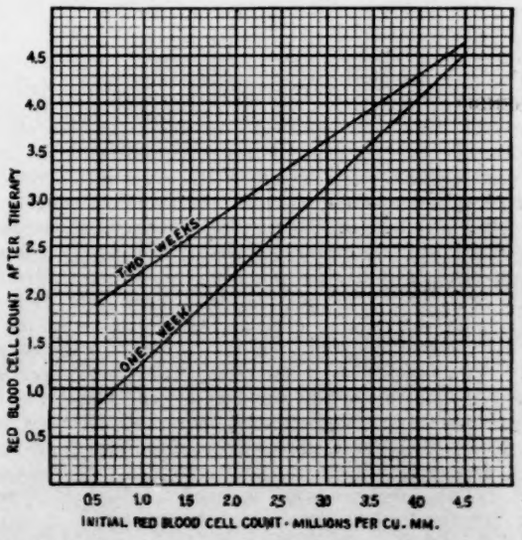

Chart 3.—The red blood cell count after one and two weeks of therapy with desiccated, defatted stomach tissue. (See example in legend for chart 1.)

SUMMARY

Standards are given for the red blood cell counts, at weekly intervals, for patients with pernicious anemia treated with liver extract intramuscularly and for desiccated defatted stomach therapy.

From the Thomas Henry Simpson Memorial Institute for Medical Research, University of Michigan.

QUININE IN MYOTONIA CONGENITA

ROBERT B. LONERGAN, M.D., AND HARRY A. PASKIND, M.D., CHICAGO

In 1936 Wolf [1] reported startling effects of quinine in states of myotonia. He treated three siblings with myotonia congenita and one patient with myotonia atrophica with quinine and found that all myotonic manifestations disappeared. He reported that 10 grains (0.65 Gm.) of quinine dihydrochloride injected intravenously abolished every myotonic phenomenon within ten minutes after administration, the effect lasting from fifteen to twenty hours. He further found that quinine hydrochloride from 5 to 10 grains (0.32 to 0.65 Gm.) given by mouth two or three times a day proved to be an adequate maintenance dose for the eradication of the myotonia.

Wolf tried the remedies previously used in such states, such as thyroid substance, atropine, posterior pituitary, calcium chloride, salicylic acid and calcium gluconate, and found them without effect on his patients. Various stimulants and depressants of the autonomic nervous system and several alkaloids he found equally ineffective.

Wolf concluded that quinine is a specific for myotonia.

Previously Lindsey and Curnen [2] presented evidence in favor of the view that the after-contraction of myotonia is of reflex origin and is due to the persistent discharge of hyperexcitable sensory end organs in muscle. It seemed reasonable to Wolf that quinine produced effects by diminishing this reflex action. Pharmacologically it had been known before that quinine produces a transient increase in strength in skeletal muscle, followed shortly by fatigue and weakness of contraction, that it produces vascular dilatation and is an antagonist to epinephrine, and that it depresses the vagus termination.

At the meeting of the American Neurologic Association in 1937 Wolf presented a paper in which he showed cinematographically the dramatic changes produced by quinine in one of his patients with myotonia.

In 1937 Kennedy and Wolf [3] reported the results of treatment with quinine in four additional patients with myotonia, three of whom had myotonia atrophica and one myotonia congenita. Again they found that quinine hydrochloride, given by mouth in doses of from 5 to 10 grains, was followed by disappearance of the myotonia. They also reported that quinine and prostigmine are antagonistic in action, quinine aggravating the symptoms of myasthenia gravis and prostigmine having the same effect in myotonia.

In discussing the pathogenesis of myotonia, Kennedy and Wolf pointed out that endocrine factors may play a part. Thus, myotonia had been observed periodically during the menses, its cessation had been observed after the birth of a child, and improvement had been noted after administration of calcium and parathyroid. As a result of experiments, Kennedy and Wolf concluded that the myotonus of myotonia congenita is a pathologic condition of the muscle or neuromuscular junction, independent of the central nervous system and, further, that quinine relieves myotonus primarily by direct action on the muscle or at the myoneural junction. They came to this conclusion after determining experimentally that spinal anesthesia does not abolish myotonia but that administration of quinine in a person previously given spinal anesthesia does abolish myotonia. They also postulated that the effectiveness of quinine in myotonia may be due to inhibition of acetylcholine production, but they felt that there were other factors at work of which there was little or no knowledge.

In another communication Kennedy and Wolf [3a] reported their experience with quinine in the treatment of myotonus extended over six cases of myotonia congenita and fifteen cases of myotonia atrophica for a period of one year. In not a single case did quinine fail to eradicate the myotonia. They found that any form of quinine, whether the hydrochloride sulfate, bisulfate or hydrobromide, was effective in doses of from 2½ to 15 grains (0.15 to 1 Gm.) by mouth two or three times a day. In only one case did symptoms of cinchonism appear, as manifested by ringing in the ears.

The only other communication we have been able to find on this subject is one by Smith [4] in which he reported that in three cases of myotonia congenita the symptoms were entirely abolished by quinine.

REPORT OF CASE

A youth aged 14 was first seen by us Sept. 6, 1937. The father had had two nervous breakdowns, characterized principally by depression, from both of which he recovered. The mother, the maternal grandfather and a maternal uncle all had a curious deformity of the little finger; the terminal phalanx did not lie in a straight line with the middle phalanx but instead made an obtuse angle with it. A sister, now 14 years of age, as far back as could be remembered had slight difficulty in starting to walk or run; the upper extremities were normal. We were not afforded the opportunity of studying the sister's case. The family history was otherwise negative.

The patient was the first born, born less than two years after marriage at full term. Labor was very difficult with face presentation, delivery by forceps and severe laceration. There was neither postnatal asphyxia nor convulsion. Infantile history was negative except that at first he gained weight poorly; only at the end of three months did he regain his birth weight. He had had only the ordinary diseases of childhood.

At 14 months he began to walk, and it was noted that for about one year he walked on his toes; this manner of walking then gradually disappeared. At 3 or 4 years the parents noticed that he had difficulty in starting movements, i. e. in starting to walk, in getting up from a sitting position, in climbing stairs and in starting to run. The parents were not aware of difficulty in the use of the hands, but in gross use of the arms, such as in throwing, they noticed the same difficulty in starting. All difficult movements would become easier with repetition, but hardly completely normal. Under conditions in which haste was required or under emotional strain, the disability was especially marked. This condition had been present since the onset. The disability was always worse in the morning or after a long rest but never completely gone at any part of the day, but it was alleviated considerably by exercise. There were no mental symptoms. The patient was a straight A student.

Examination disclosed the typical herculean musculature so often seen in this condition. This was especially pronounced in the quadriceps group, but the muscles of the calf, shoulder girdle, arms, back and neck also showed herculean conformation. Myotatic irritability was marked; striking with a hammer produced a furrow over any part of the skeletal muscles. The myotonic disability was easily demonstrated; there was difficulty in starting to walk, to run or to climb stairs and in squatting or getting up from a squatting or sitting position. The disability was present but less evident in the upper extremities and here was most marked in the hands and fingers; there was difficulty in grasping or shaking hands. In all affected parts the disability diminished but did not disappear after several attempts. The muscles innervated by the cranial nerves were spared; there was no difficulty with the muscles of expression, mastication, deglutition and none with the extra-ocular movements and tongue. Sensation was intact. All deep reflexes were diminished; plantar and abdominal reflexes were normal. Examination of the cranial nerves yielded negative results.

The patient had a high narrow palate, two colored irides, brown speckled with blue, and deformed fingers like those described in the mother and other members of the mother's family.

The basal metabolic rate was normal. Examination of the blood, the Kahn test on the blood and chemistry of the blood yielded negative results.

A diagnosis of myotonia congenita was made.

The patient was given quinine sulfate 5 grains three times a day. This produced improvement at once but not eradication, and increasing dosages had the same effect, i. e. amelioration only, until 10 grains was given five times a day, when disappearance of the myotonic phenomena occurred. With this

From the Departments of Orthopedic Surgery and Nervous and Mental Diseases, Northwestern University School of Medicine and the Evanston Hospital.

1. Wolf, Alexander: Quinine: An Effective Form of Treatment for Myotonia, Arch. Neurol. & Psychiat. **36:** 382-383 (Aug.) 1936.

2. Lindsey, D. B., and Curnen, E. C.: An Electromyographic Study of Myotonia, Arch. Neurol. & Psychiat. **35:** 253-269 (Feb.) 1935.

3. (*a*) Kennedy, Foster, and Wolf, Alexander: Quinine in Myotonia and Prostigmine in Myasthenia, J. A. M. A. **110:** 198-201 (Jan. 15) 1938; (*b*) Experiments with Quinine and Prostigmine in Treatment of Myotonia and Myasthenia, Arch. Neurol. & Psychiat. **37:** 68-74 (Jan.) 1937.

4. Smith, W. A.: Quinine Treatment of Myotonia Congenita, J. A. M. A. **108:** 43 (Jan. 2) 1937.

dosage, starting to walk, run, sit up, run upstairs, shake hands and the like presented no difficulty. He was kept on this dosage for one week. After this the dosage was gradually diminished until he took one dose of 15 grains at 7 a. m. This eradicated the hypertonia until 6 p. m., and if his evening's activities required easy movements he took another 10 grains at 6 p. m.

He was last seen in August 1938. At that time he continued free from myotonic symptoms during the day if he took 15 grains of quinine sulfate in the morning, and this freedom from myotonic symptoms was continued throughout the evening if he took 10 grains more after supper.

On only two occasions were symptoms of cinchonism present in the form of ringing in the ears for short periods, and then only when he was getting 50 grains (3.2 Gm.) of quinine sulfate a day.

CONCLUSION

In a case of myotonia congenita we have been able to confirm the value of quinine as reported by Wolf, Kennedy and Wolf, and Smith.

25 East Washington Street.

Special Article

CONFERENCES ON THERAPY

I. TREATMENT OF PAIN

NOTE.—*These are actual reports, slightly edited, of conferences by the members of the Departments of Pharmacology and of Medicine of Cornell University Medical College and the New York Hospital. The questions and discussions involve participation by members of the college staff, students and visitors. The next report will concern "The Treatment of Coronary Disease."*—ED.

DR. MCKEEN CATTELL: These conferences were inaugurated as a joint undertaking of the Departments of Medicine and of Pharmacology with the idea of stimulating interest in rational therapeutics. Representatives from the clinical departments and from the laboratory departments lead the discussion. Free and informal discussion represents the most important part of these conferences.

DR. HARRY GOLD: The symptom pain stands high, if it does not actually lead, the list of causes of disability. It is probably the most frequent symptom requiring attention in the practice of medicine. If one were to survey a fair sample of the results generally obtained with drugs for the treatment of pain, one would discover that they are not as good as they might be. The outstanding deficiencies fall into two classes:

1. First, one finds a considerable proportion of failures to abolish the pain. The primary objective seems often not to be attained.

2. Second, in a fair proportion of cases, whether the pain is controlled or not, other effects, disagreeable and sometimes disastrous, result: nausea, vomiting, constipation, distention, urinary retention, temporary blindness, deafness, skin eruptions, profuse perspiration, stupor, methemoglobinemia, agranulocytosis, acute yellow atrophy of the liver, and narcotic addiction. This is but a partial list of one that could be very much more formidable, representing the untoward reactions that follow the use of agents employed for the relief of pain.

All of this indicates that there are no ideal pain-relieving substances; our task is to consider what we need to do in order to make the drugs or medicinal agents at our disposal as effective and as safe as possible in the control of pain.

Every case of pain presents a problem. The use of drugs to control pain involves a judgment which grows out of the careful appraisal of many facts. There is a prevailing tendency in a case with pain to dig down into our bag of analgesics, fetch up something that is supposed to kill pain, and prescribe. If we do that, the range of successful treatment becomes relatively small indeed, and alongside of the little good that we do, in that way, there stands enough harm to eclipse it. Illustrations of these remarks will appear in matters that will be discussed presently.

What are the matters one needs to consider as a basis for the use of drugs in the treatment of pain, in a manner likely to yield the greatest returns with the least risk?

1. Pain is a symptom and not a disease. In our zeal to relieve it, or in our success in relieving it, there is always the danger of overlooking the less obvious and less dramatic aspect of the case, the disease itself. Recently I encountered the case of a nurse who had suffered attacks of thoracic pain. With the approval of the house officer she took large doses of an analgesic agent and obtained relief. The last attack did not respond as effectively as the previous ones, whereupon a careful examination was made. The results showed that she had been carrying on her nursing work with a pleural effusion and active pulmonary tuberculosis. This is the sort of thing one occasionally encounters. We must bear this fact in mind constantly, that pain is a symptom and not a disease, if the relief of pain is not from time to time to prove to be a misfortune.

2. Pain labels a disease and its location. This is another fact of some importance and is closely related to the statement previously made. You have all probably heard about cases, or perhaps you know of some from your own experience, of peritonitis directly attributable to the overzealous relief of abdominal pain before a definite diagnosis has been made.

3. The cause of pain is important to determine. We all know that it is necessary to ascertain whether the cause of a headache is a brain tumor or some insignificant functional disturbance so that the cause (the tumor) may be removed. But I have in mind something less than that. From the standpoint of relief alone without removal of cause, a clear appreciation of the cause is often very helpful. For example, of three kinds of pain in the chest, the pain of intercostal neuralgia, the pain of effort angina and the pain of coronary thrombosis, differentiation is sometimes extraordinarily difficult. The agents which relieve one may be ineffective in the other. One can group other types of pain in that way; for example, pain in the legs due to myositis, vitamin B_1 deficiency or vascular disease. The effectiveness of the relief of the pain aside from the question of removing the cause depends here on a differential diagnosis.

4. The pathogenesis of pain is a matter of some importance; whether, for example, the pain is caused by spasm of smooth muscle or anoxemia or comes about as the result of inflammatory reactions around nerve fibers or endings.

5. The severity of the pain ought to be considered. Perhaps it is not sufficiently severe to require relief by therapeutic agents. Not infrequently when you are about to prescribe for a patient with pain the patient will ask you what the medicine is for, and you will say "For your pain." He may reply "I don't like medicines. I am not much interested in the relief of the pain so long as my mind is relieved that the cause is not

serious." Before we prescribe a drug, the question should be put whether the relief will recompense the patient for other forms of discomfort which the drug may cause. You will see patients taking two or three doses of codeine a day for the relief of very mild anginal pains. The price is disagreeable stupor and troublesome constipation. Such pains can often be much better controlled if we take the trouble to assist patients in making the necessary adjustments to reduce their activities to a level within their capacity without pain.

6. The natural course of the pain is also significant: Is it going to last a few hours or several days? Is it going to recur over long periods of time? Is it the kind of pain the intensity of which is likely to fall from its peak very gradually or is it likely to subside very abruptly? Morphine poisoning often arises from the use of large doses of the drug in patients in whom severe pain subsides abruptly. In such a case the morphine may seem to be producing very little depression, and the doses are repeated to secure more relief of the pain. With little warning, however, you find the patient lapsing into a state of profound stupor with depressed respiration, and you wonder what has happened. You have used large doses of morphine in a variety of pain which tends spontaneously to come to an end rather abruptly, leaving the patient under the influence of an amount of morphine which is toxic in the absence of pain, for pain is an antidote to morphine!

The More Common Analgesic Agents

A. Raise Thresholds	5. *Salicylates*
1. *Opium Group:*	6. *Magnesium Sulfate*
Morphine	7. *Sedatives*
Codeine	*B. Relax Smooth Muscle*
Dilaudid	1. Nitrites
Pantopon	2. Xanthines
2. *Coal Tar Derivatives:*	3. Atropine
Acetanilid	4. Papaverine
Acetophenetidin	5. Calcium
3. *Pyrazolon Compounds:*	*C. Special Mechanisms*
Antipyrine	1. Trichlorethylene
Aminopyrine	2. Ergotamine
4. *Cinchoninic Acid Group:*	3. Caffeine
Cinchophen	4. Vitamin B_1
Neocinchophen	

7. The psychic element in pain may vary anywhere from an insignificant role to the sole cause of the pain. That needs to be considered also from the standpoint of the kind of analgesic agents that are to be used. Fear and anxiety increase the perception of pain, and the use of small doses of sedatives greatly enhances the effectiveness of some of the analgesic agents. When reasonable procedures in a given case seem to be without influence on the pain, one might well ask whether the patient wants his pain relieved; the pain in this case may be one of the patient's most precious possessions. That needs to be considered before one goes on increasing the doses of drugs or shifting from one preparation to another in the endeavor to relieve it.

8. Finally, drugs are only adjuvants in the treatment of pain. Physical therapy, psychotherapy and specific cause treatment in the long run play the most important role in any program in which pain is the center of interest.

These are some of the important questions demanding consideration before one writes a single word of a prescription for the treatment of pain. We must not pretend, of course, that a clearcut answer will be always forthcoming, but I feel sure that if we ask those questions often enough we shall obtain a sufficient number of answers to make this sort of procedure extremely profitable.

Here is a list of the more common analgesic agents. It is not possible to make an altogether satisfactory classification of them. Perhaps this is as good as any, but you may think of a better one. The first group includes those agents which raise thresholds at the centers and block the perception of pain. The second includes those which relax smooth muscle and in that way abolish the impulses at their source. The third group includes substances which exert a specific action on certain kinds of pain: trichlorethylene, ergotamine, caffeine, vitamin B_1. In some of these the mechanism is quite well established, in the case of others our knowledge is imperfect.

The more common clinical varieties of pain which present special problems are (1) headache, (2) visceral pain, (3) cardiac pain, (4) neuralgias, (5) root pains, (6) chronic arthritis, (7) dysmenorrhea, (8) labor pain. The list is not complete. We do not have the time this morning to go into all of these matters. Dr. Wolff is going to discuss some of the types of pain, and if any one has any special interest in others a discussion may be provoked by asking questions.

DR. CATTELL: Dr. Wolff will now take up the management of a specific type of pain.

DR. HAROLD G. WOLFF: I am going to discuss one type of pain, and that is headache; and just one variety of headache, namely migraine. I am selecting migraine to talk about for two reasons: 1. It is said to be the commonest clinical entity that civilized man happened to fall heir to. 2. I think that the management of migraine headache allows us to discuss the clinical approach to the problem of pain in general.

By migraine headache I mean the type of headache that is usually unilateral in onset, may become generalized, is associated with nausea and vomiting, sometimes with visual and other sensory disturbances, and usually occurs in families.

There are three ways of approaching this type of headache, as there are for other types of pain: first, by considering agents or procedures that act at the site of production of pain, for instance ergotamine tartrate, ergonovine, ephedrine, benzedrine, epinephrine, solution of posterior pituitary, ice cap, surgical ligation, resection and mechanical pressure; second, agents or procedures that act by raising the threshold of pain as, for example, codeine, morphine, acetylsalicylic acid, aminopyrine, acetanilid, phenacetin, ice cap; third, agents or procedures that act by lowering the blood pressure as in the case of glyceryl trinitrate or acetylcholine. I will disregard this third classification and limit our discussion to the first two.

Migraine results from the distention of some of the cranial arteries, chiefly the branches of the external carotid artery.

We know from our studies in the laboratory that a generalized headache can be produced with histamine, but after resection of the first division of the fifth cranial nerve such a headache will not appear in the part of the patient's head innervated by this division of the fifth nerve. Thus for clinical purposes we may consider the chief afferent pathway for headache to be the first division of the fifth nerve.

The method of investigation was as follows: The patient with a headache is put on a stretcher in a darkened room and a tambour over his temporal artery on the affected side records the amplitude of pulsations of the arterial walls. Records are made on a moving film in a camera.

In a representative patient with a migraine headache, ergotamine tartrate was given intravenously, and in the course of the next ten minutes the pulsations of the branches of the external carotid as recorded from the temporal artery had been reduced by 50 per cent and the headache had disappeared.

In another patient who received ergotamine tartrate (0.5 mg. intravenously) it happened to take about forty minutes for the headache to disappear, but again a parallel between the decline in the amplitude of pulsations of the temporal artery and intensity of the headache was demonstrated. A photograph was taken of this patient during the period of his headache, showing the large temporal vessels, both arterial and venous, standing out, which was in striking contrast to the flattened appearance of these vessels in a photograph taken immediately after the ergotamine had had its effect.

Records of pulsation of the cerebrospinal fluid, which represents the activity of the major spinal and the intracranial vessels, show variations in the height of pulsation which do not appear to be correlated with the headache or the disappearance of the headache after administration of ergotamine tartrate. Similarly, we have been able to demonstrate no correlation between the pressure of the spinal fluid and the headache. Thus I think we are at the moment justified in saying we do not know what role the branches of the internal carotid artery play in migraine headache, but such evidence as we have indicate it is not too important a role.

Photographs were taken of the retinal vessels before and after the administration of ergotamine tartrate. Although the veins appear to be a little smaller, I doubt whether there is much change in the arteries, although there may be a slight constriction.

Further, it can be demonstrated that ergotamine tartrate does not act in terminating headache by raising the threshold to pain. For instance, in one patient who had had his headache terminated by an intravenous dose of ergotamine tartrate an injection of 0.1 mg. of histamine produced the usual acute, the short-lived, histamine headache. This then indicates that the patient is just as able to perceive the headache after the administration of ergotamine as he was before.

In one patient the intramuscular injection of solution of posterior pituitary caused the headache to disappear, but the patient was white, was tremulous, complained of bad abdominal cramps and bad precordial pain, and I feared he might faint during the experiment. It is not a drug that one would care to give regularly, and it is not one that one can count on having a constant effect. It is not to be recommended.

Ephedrine sometimes succeeds in improving or eliminating a migraine headache, via the same mechanism: a reduction in the amplitude of pulsation of the cranial arteries. But the patient to whom it is given for migraine headache becomes tense and tremulous, and the disappearance of pain is often transient since at the end of four hours the headache may return with full intensity. Therefore, ephedrine cannot be considered as either a practical or a useful means of treating migraine headache.

In our experiments ergonovine, when successful, also eliminated headache by the same mechanism as did ergotamine tartrate. It contains more of the oxytoxic property of the ergot drug, will abolish headaches in only about 50 per cent of trials, and cannot be relied on to be 100 per cent effective in reducing the amplitude of pulsations of cranial arteries.

Thus, if the agent employed succeeds in reducing the amplitude of pulsation of the cranial arteries by a sufficient amount, i. e. from 40 to 50 per cent, headache will be completely abolished, as is the case with ergotamine tartrate. It is thus evident that ergonovine hydracrylate cannot be regarded as an important asset in the treatment of migraine headache. Benzedrine sulfate, caffeine with sodium benzoate and pitressin are likewise unreliable in their effect on the magnitude of cranial artery pulsations and consequently in their effect on the headache. For instance, in two patients, caffeine with sodium benzoate (0.5 mg. intravenously) happened to increase the amplitude of pulsations and made the headache worse. Ergotamine tartrate subsequently reduced the pulsations by 40 per cent and eliminated the headache. Similarly, benzedrine sulfate reduced the amplitude of pulsations in another patient 25 per cent without reducing the headache, whereas ergotamine tartrate subsequently administered terminated it, and the amplitude of pulsations was seen to be reduced by 50 per cent. Ergotamine tartrate may at the moment be regarded as the most effective agent we have in reducing the amplitude of pulsations of the cranial arteries and terminating the migraine headache attack.

Before ergotamine tartrate was available, codeine was the best agent for stopping headache. One grain, or 60 mg., of codeine will stop most headaches, but how does it work? We observed a patient with migraine headache to whom 60 mg. of codeine was administered subcutaneously. As the headache disappeared the amplitude of pulsation of the cranial arteries did not change at all, an illustration that codeine does not act on the local pain-producing mechanism but raises the threshold to pain impulses arising from the stretched and dilated cranial vessels.

Codeine administered to another patient abolished his headache, again with no change in the amplitude of cranial artery pulsations. This patient soon complained that his headache had returned with about 50 per cent of its original severity. We then gave him ergotamine tartrate, the headache disappeared promptly, and the cranial artery pulsations, although they had not changed during this whole period when the headache had been transiently relieved by codeine, were now reduced in amplitude by over 50 per cent. His migraine attack proved to be successfully terminated.

How should one manage an acute migraine attack? The patient should retire to a darkened room and remain in bed for at least two hours, and 0.5 mg. of ergotamine tartrate should be given intramuscularly as soon as it is feasible to give the drug after the onset of the headache. This drug when given intravenously will produce quicker results; that is, it takes about thirty to fifty minutes to produce effects through the intramuscular route and about ten to forty minutes by the intravenous route. Giving ergotamine tartrate by the mouth should be avoided for two reasons: 1. It eliminates the headache only about 50 to 60 per cent of the time. 2. Patients may be induced to take it too often. Patients may have the tendency to take a few pills by mouth "every once in a while." If it is necessary to give it by mouth for reasons best known to you at the time, give 3 mg. followed by 2 mg. an hour until the headache has disappeared or a total of 11 mg. has been given. However, I am not enthusiastic about this procedure.

Suppose the patient feels as though he is about to have a migraine attack, is there anything you can do

to stop it from developing? Usually not, but you might try. The patient can be urged to go to bed and 3 mg. of ergotamine tartrate may be placed under the tongue. This will be absorbed in a few minutes and sometimes will stop the headache when repeated in 2 mg. doses hourly until 11 mg. has been given. If it does not, you are in a dilemma because you have already given ergotamine tartrate and you do not know how much more to give by the more successful intramuscular or intravenous route. I am not in favor of ergotamine tartrate by mouth. Some report the successful use of a mixture of acetanilid and sodium amytal, although I never used it and I do not know how effective it is. In any event the patient should stay in bed for two hours after such medication. Many times patients feel they are going to get a headache and don't, so you never know whether this kind of procedure is efficient or not, but you can try it and see what happens.

Don't give ergotamine tartrate more often than once a week to patients with cardiovascular disease, with or without hypertension, including those with Raynaud's syndrome, venous thrombosis, syphilitic arteritis and coronary disease; to patients with sepsis or fever; to patients with hepatic or renal disease; to pregnant women. Fortunately, most pregnant women stop having migraine attacks during their pregnancy, and the occasional woman can take ergotamine late in the pregnancy without danger; but never give ergonovine hydracrylate under any circumstances to a pregnant woman. Lastly, do not give ergotamine tartrate to badly nourished or cachectic persons. It is said that persons deficient in vitamin C do badly with ergotamine, and a poorly nourished person probably has such a vitamin deficiency. Finally, remember that in treating migraine headache you are treating the acute episode of pain and not the syndrome of migraine.

STUDENT: What is the length of time that a patient with migraine gets relief from one injection of ergotamine?

DR. WOLFF: It terminates the attack. Attacks usually last from a few hours to a few days. The administration of ergotamine does not shorten the interval between attacks. The management of the frequency of these various attacks must be through other means than ergotamine. Ergotamine simply terminates any given attack.

STUDENT: I should like to know the mode of action and effectiveness of trichlorethylene.

DR. WOLFF: Trichlorethylene is useful in pains of the face of any kind. It is not known what the exact site of action is, but it seems to raise the threshold for all types of pain about the head. Its chief usefulness is in trigeminal neuralgia. I think that was discovered, as you probably know, during the war when it was used as a solvent for certain airplane coverings, and the workers in the airplane factories were being poisoned, so that they became anesthetic about the face.

STUDENT: Has it any effect on pains elsewhere?

DR. WOLFF: I do not believe so but I am not certain.

DR. CATTELL: In the past we have been fortunate in having the collaboration of representatives from various clinical departments in connection with our conferences. The list that was put on the board by Dr. Gold includes a number of conditions which might be discussed further. I wonder if there is any one here from the Department of Obstetrics and Gynecology who might be willing to say something about the topics dysmenorrhea and labor pain. The question of arthritis is another important topic.

DR. ANDREW A. MARCHETTI: I will talk about the first one. Dysmenorrhea is the pain in menstruation. As you know, dysmenorrhea is either congenital, functional or acquired. I think that of course the most important thing to do is to find out what can ease dysmenorrhea. Most of the time our therapy is pointed toward patients with dysmenorrhea who have either hypoplastic, that is, more or less infantile, generative organs or a malposition, acute anteflexion and acute retroflexion. In those instances we give them so-called compound powders of atropine and codeine. Each powder contains 16 mg. of codeine sulfate and 0.25 mg. of atropine sulfate, as well as 160 mg. of acetylsalicylic acid and acetophenetidin. Patients are usually instructed to take the powders every four hours when they expect the pain, and usually two or three will relieve pains which are associated with the menstrual period. In instances we have used codeine, but as a rule that does not do as well as the compound powders of atropine. As Dr. Gold pointed out, the atropine is supposed to bring about relaxation of smooth muscle. It does help, especially in case of acute anteflexion. It is not 100 per cent effective, of course, and it is less effective in the patient with a hypoplastic uterus.

Some of the nitrites have been used for dysmenorrhea, but I do not believe they are used as commonly as atropine and codeine.

In the acquired dysmenorrhea it may be a uterine or ovarian tumor, an inflammatory disease or a flare-up of salpingitis which causes the pain. Peritoneal or abdominal tumors that press on the uterus itself cause pain which is not elicited until the patient is about to have a period. A uterine or ovarian tumor may cause pain in the intermenstrual period.

Then too the cachectic or the undernourished person may complain of dysmenorrhea. You will find them anemic, and when they are built up by good food, fresh air, and the things we commonly have at our disposal for nutritional disturbances, usually the pain at menstrual time disappears.

Are there any questions that you wish to ask?

DR. GOLD: I wonder how deep is the conviction with regard to atropine for easing menstrual pain. A quarter of a milligram is a mighty small dose, and I am not sure that with such a dose it will be ever possible to demonstrate any physiologic effect.

There is a question I should like to ask as to codeine. Are you ever worried about the possibility of drug addiction since these patients take it repeatedly over long periods of time?

DR. MARCHETTI: I have never seen that. I know Dr. Kelly in Baltimore is very apprehensive about drug addiction. I asked him about it and he said he had never seen it except on one or two occasions when patients became addicted to codeine. The drug is only a temporary measure. Usually, if the dysmenorrhea is severe enough, whether it is acquired, functional or congenital, the patient comes back. In the malpositions, let us say, we insert a pessary and give the patient a therapeutic test. If the retro position is relieved by putting the uterus in its normal position or approaching that, we then know the cause of the dysmenorrhea and eventually the patient will get a suspension.

DR. GOLD: I understand that aminopyrine is widely used in dysmenorrhea. Would you care to comment on this?

DR. MARCHETTI: We discourage its use, particularly because of the danger of agranulocytosis. It does relieve the pain but not as effectively as the compound powder of atropine and codeine.

DR. CATTELL: We have a small amount of time remaining for discussion, and there may be questions relating to some of the specific conditions mentioned. It seems to me this is an unusual opportunity to ask questions of men who have given special thought to the particular problems under discussion, and we should like to have all the students participate.

STUDENT: I have heard of the use of benzyl benzoate in dysmenorrhea, and I was wondering whether there was anything to it.

DR. MARCHETTI: It helps in some instances. I do not think it is as effective as the codeine and atropine.

STUDENT: I should like to ask Dr. Gold how large a dose of morphine may be given to control pain in coronary thrombosis.

DR. GOLD: You cannot give more than a quarter of a grain of morphine ever entirely safely. One gives as high as three quarters of a grain or even a grain, but if so one may expect to get into serious difficulties at times because coronary thrombosis is a classic illustration of very severe pain which tends to descend from its peak rather abruptly. If you give a quarter of a grain and the pain is not relieved, then within a half to three quarters of an hour you give another quarter and another quarter; perhaps by the third or fourth dose the pain may subside rather abruptly and at the same time you have a patient in fairly deep narcosis, in whom the pain had previously served as the antidote to the toxic effects of the morphine.

DR. CATTELL: I should like to ask Dr. Angevine whether there are some points in the management of arthritis that it might be profitable to discuss.

DR. D. MURRAY ANGEVINE: I think practically every drug has been used in the treatment of arthritis. I will mention just two types, rheumatoid arthritis and osteo-arthritis. The latter is apparently not related to infection. The ideal treatment for arthritis, just as for rheumatic fever, is rest. Sometimes it is impossible to provide rest, so we must do the best we can. We find that salicylates are of value in arthritis, but I think that is a rather general statement. We all use them because we know of nothing better, but practically 60 per cent of the patients that I see in the clinic will say "I took aspirin, but it did not help me." Rheumatic fever, of course, is an entirely different proposition. Our big agent for the treatment of arthritis, aside from rest, is physical therapy, and there are numerous methods by which it can be applied.

There are two points that may be of interest. It has been observed that patients with rheumatoid arthritis who became jaundiced become free from pain. This has been applied experimentally and about one half of the people who are jaundiced artificially are free from pain. It is obvious that such a method cannot be generally applied. However, such an observation is of value in that it may give us an indication as to the mechanism of pain in arthritis. In view of Dr. Wolff's statement that pregnancy relieves migraine it is of some interest that in a series of thirty pregnancies in patients with rheumatoid arthritis practically all were relieved of pain during their pregnancy. In fact, one woman said that she had gone through four pregnancies, and during them she was entirely relieved of her arthritis.

DR. ARTHUR P. RICHARDSON:[1] Pain is, of course, without a doubt the principal reason for patients coming to doctors. It is the thing that patients usually want to be relieved of. They are not particularly interested in what the mechanism is, all they want is relief from their pain. I am not at all sure of the quotation of Pasteur, but I believe it runs like this: "We would cure few, relieve many, and comfort all." That is beyond doubt the outstanding duty of all doctors, at least from the point of view of the patient.

DR. JOSEPH C. HINSEY: I have been concerned with mechanisms involved in pain rather than with drug effects on pain. However, I have been very much interested in this discussion. There are two or three points that occur to me. First, in the use of drugs which raise the threshold to pain, we are dealing with effects on peripheral or central mechanisms, and probably both. It should be emphasized that the peripheral pathways traverse the dorsal roots of spinal nerves and the sensory roots of cranial ones. There are no afferent pathways aside from these.

In dealing with drugs which attack the efferent nervous mechanisms or smooth muscle directly, the phenomenon of relaxation of smooth muscles is a very important factor in the relief of pain. In Dr. Wolff's description of the relief of migraine by ergotamine tartrate and other drugs, the pulsations in the branches of the external carotid artery were reduced. I do not know what changes in the state of the smooth muscles of the arterial walls accompanied this reduction. However, in conditions in which pain is produced by anemia and the resultant anoxia in tissues, relaxation of smooth muscle in the vascular bed induced by the action of drugs leads to an improvement of blood supply and helps to relieve pain. In physical therapy, counter-irritation may relieve pain by the induction of reflexes that relax smooth muscle both at the periphery and in the viscera, producing among other things an improvement of blood supply.

Second, there is one other place where drugs are used in the problem of pain that is of interest at the present time; that is, in the field of diagnosis. The use of local anesthetics in the blocking of peripheral and visceral nerves gives information as to the possible relief to be obtained in painful syndromes by surgical procedures. Recently, Livingston has reported ten cases of atypical pain in the extremities produced by trivial injuries. He found that he could relieve pain by the use of local anesthesia at the periphery in the "trigger" zones and also by blocking the sympathetic trunks. It seems to me that the use of local anesthetics such as procaine hydrochloride has an important role in the attack on a number of types of atypical pain.

1. Dr. Richardson is National Research Fellow, the Johns Hopkins University.

Political Career of Claude Bernard.—The year 1860 saw the beginning of Bernard's political career, which was, indeed, short but which occurred at an exciting moment in the history of his country. An imperial decree of May 6 made him a senator. His yearly income was in consequence augmented by 30,000 francs and there is still among his relics at Saint-Julien a card bearing five stamps, which shows that he received five quarterly payments of his stipened. . . . Bernard took his duties as senator seriously, as he did all obligations which he assumed. There is not a day's balloting recorded in the official journal after Bernard took his seat in August 1869 which does not include his name.—Olmsted, J. M. D.: Claude Bernard, Physiologist, New York, Harper & Bros., 1938.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING ARTICLE AND REPORT.

HOWARD A. CARTER, Secretary.

PHYSICAL CHARACTERISTICS OF SHORT WAVE DIATHERMY

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In former articles[1] the physical and biophysical aspects of the older type of long wave diathermy have been discussed. These previous articles contain descriptions of the methods whereby the low frequency 25 to 60 cycle alternating current may be converted into high frequency diathermy current by means of the spark gap diathermy machine or the vacuum tube apparatus. This older type of diathermy current is that which has a frequency between 500 and 2,000 kilocycles per second and is applied to the patient by contact electrodes. Since a discussion of long wave diathermy has already been given, and since the main interest today is in short wave diathermy, the present article will be confined almost exclusively to short wave diathermy except when comparisons are to be made with the older form of diathermy.

It is of historical interest that during the past year a friendly controversy has arisen as to the priority of the discovery that high frequency alternating electric currents could traverse irritable tissues without electrical shock. The clinical use of diathermy as a mode of therapy followed soon after this discovery. According to Bordier,[2] d'Arsonval, Claude Bernard's successor at the University of Paris, commenced in 1881 a study of the stimulating effects of electric currents of varying frequency. d'Arsonval built an oscillator capable of producing alternating currents of frequencies as high as 10,000 cycles a second and demonstrated to his classes at the university in 1889 that at the higher frequencies the current for stimulation had to be increased. Following the discoveries of Hertz, d'Arsonval used the hertzian oscillator (the spark gap circuit) for frequencies above 10,000 cycles. These results were published in 1891 and first presented at meetings of the Society of Biology at Paris at its sessions of Feb. 24, April 25 and May 2, 1891. Nikola Tesla, an Austrian physicist in the United States, was studying illumination produced by high frequency currents and noted that high frequency currents of sufficient intensity to cause illumination did not produce neuromuscular stimulation. These observations of Tesla were published May 23, 1891. The conclusion to be drawn from this interesting note of Bordier's is that the discoveries were made almost simultaneously and were published in 1891. This year may be regarded as the beginning of the development of diathermy.

1. (*a*) Hemingway, Allan, and Stenstrom, K. W.: Physical Characteristics of High Frequency Current, J. A. M. A. **98**: 1446 (April 23) 1932; (*b*) Physical Characteristics of Diathermy and Short Wave Diathermy Machines, ibid. **105**: 1424 (Nov. 2) 1935.

2. Bordier, H.: Tesla or d'Arsonval? Arch. Phys.. Therapy **19**: 109 (Feb.) 1938.

SHORT WAVE DIATHERMY

Since 1930 there has arisen a continuously increasing interest in short wave diathermy, stimulated by many clinical reports of its beneficial therapeutic use and a large amount of advertising by manufacturers of apparatus. This new form of therapy has been greeted with much enthusiasm by some investigators as a discovery of major importance. The *British Journal of Physical Medicine*[3] states "It is no exaggeration to call short wave diathermy the greatest discovery in physical medicine since the work of Roentgen." Other investigators, particularly those in America, have been less enthusiastic about the merits of short wave diathermy and believe it to be solely a unique and useful method of applying heat. Conventional diathermy, or long wave diathermy, has been used with success for many years and short wave diathermy can be regarded only as a new and improved mode of therapy if it has definite proved advantages over the older type. It is our purpose in this review to describe the method of production of short wave currents and then to discuss the advantages and disadvantages of the newer form of diathermy in comparison with the older form.

A TYPICAL OSCILLATOR CIRCUIT

There are several typical circuits for the generation of short wave diathermy currents. These may be divided into two groups: those which produce the longer of the short wave diathermy currents, i. e. frequencies in the range from 10 to 100 megacycles (from 30 to 3 meters), and a second group producing frequencies greater than 100 megacycles. As a typical oscillator of the first group, the simple two-tube "push-pull" circuit will be described. This type of oscillator for production of long wave diathermy currents (1 megacycle per second) has been described by Hemingway and Witts.[4] The same typical current may be used for the generation of higher frequencies.[5] This entire circuit can be considered to consist of three essential parts, (*a*) the power supply, (*b*) the oscillating circuit and (*c*) the output circuits.

(*a*) *The Power Supply.*—The high frequency current in short wave diathermy machines is generated by a vacuum tube oscillator circuit which usually consists of one or two vacuum tubes with an appropriate circuit of inductances and capacities. The thermionic vacuum tubes are evacuated glass bulbs containing a filament, grid and plate. The filament is heated to incandescence by a low voltage alternating current of the same frequency as the input current, i. e. from 25 to 60 cycles per second. A high direct current voltage of from 100 to 1,000 volts is applied between plate and filament, the plate being made positive and the filament negative. It is the function of the power supply to furnish the low frequency low voltage alternating current to heat the filament of the vacuum tubes and to supply the high direct current voltage to draw electrons from the filament to the plate. The power supply unit consists of one or two transformers, two or four rectifier vacuum tubes and sometimes a condenser. For simplicity a four tube rectifier will be described, but this may be

3. The Greatest Discovery, editorial, Brit. J. Phys. Med. **8**: 127 (Dec.) 1933.

4. Hemingway, Allan, and Witts, G. H.: A High Frequency Apparatus for Producing a Measured Heat Stimulus in Studies of Physiological Temperature Regulation, Physics **7**: 299, 1936.

5. Bishop, F. W.: An Apparatus for the Production of Local Heat in Body Tissue by Means of High Frequency Electrical Fields, Radiology **21**: 487 (Nov.) 1933.

replaced by one with two tubes which functions as the described four tube type.

One transformer converts the 110 volt 60 cycle current to low voltage 4 to 10 volt 60 cycle current to heat the filament of the vacuum tubes. This is a "step-down" transformer. The other one is a "step-up" transformer and converts the 110 volt 60 cycle current into from 500 to 1,000 volt 60 cycle current. This high voltage current in some machines is "rectified," as will be described, or in other machines is delivered as high voltage alternating current to the oscillator tubes.

The rectifier system, if present, consists of two or four rectifier tubes. A four tube rectifier is shown in figure 1 and consists of four diode tubes. The two tube rectifiers function in the same manner but two tubes are combined into one. These diode tubes each contain a filament and plate and permit electrons to flow only in one direction—from filament to plate—and in this way behave as thermionic valves. An electron current flows only when the plate is positively charged with respect to the filament. When the plate is positive the negatively charged electrons which are emitted by the filament move to the plate, the stream of particles forming the current. When the filament is made positive and the plate negative no current flows, since the current through the tube is carried only by the negatively charged electrons. In figure 1 the arrows indicate the direction in which the current flows through the tubes. A high voltage alternating current is supplied to the rectifier system by the step up transformer. This current, which passes through meter M_1, is indicated at

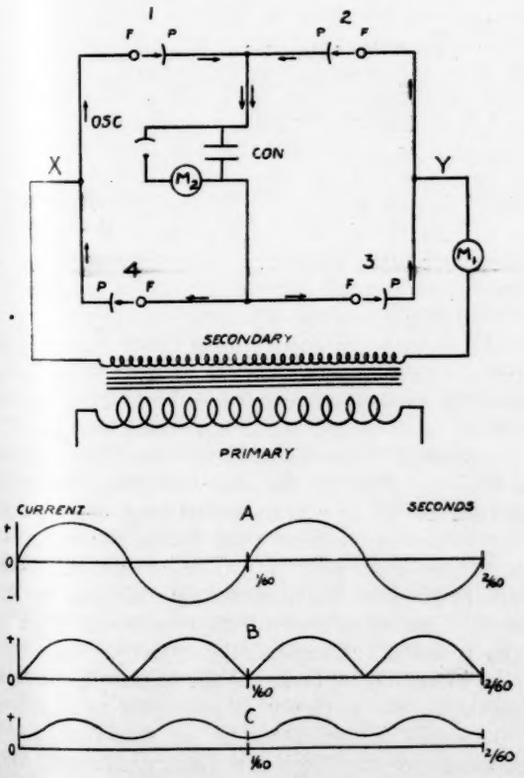


Fig. 1.—Action of full wave rectifier in power supply unit of an oscillator. *F P*, filament and plates of rectifier tubes, 1, 2, 3, 4. *Osc*, vacuum tube in oscillator circuit to which rectifier supplies a high direct current voltage output. *Con*, condenser of high capacity connected in parallel with direct current output of rectifier. *A*, alternating current from transformer secondary as indicated in ammeter M_1. *B*, rectified current flowing in output circuit as measured in ammeter M_2 without condenser (*Con*) in circuit. *C*, output current from rectifier as measured in M_1 with condenser (*Con*) connected as shown.

curve *A*. The positions *x* and *y* are subjected to an alternating potential, which varies in a cyclic manner. When *x* is positive *y* is negative and $\frac{1}{120}$ second later *x* is negative and *y* is positive. When *x* is negative and *y* is positive the electron current flows over the path $x \rightarrow 1 \rightarrow osc \rightarrow 3 \rightarrow y$ and no current flows through tubes 2 and 4 on account of the electronic action of the valve. During the next half cycle when *x* is positive and *y* negative the current flows over the path $Y \rightarrow 2 \rightarrow osc \rightarrow 4 \rightarrow X$ and no current flows through tubes 1 and 3. In both instances the current from the rectifier, that is, the current supplied to the oscillator (*osc*) and measured by meter M_2, flows in one direction. Without the condenser (*con*) the unidirectional current from the rectifier would pulsate as shown in curve *B*. The presence of the condenser (*con*) smoothes out the pulsations to give an output current as indicated by curve *C*. The condenser acts as a storage place for the electrical charges that enter and leave while rapid changes of current are taking place. This condenser has a tendency to produce a uniform flow in much the same way as that in which the elastic walls of the large arteries take up the pressure pulse and produce an even flow of blood.

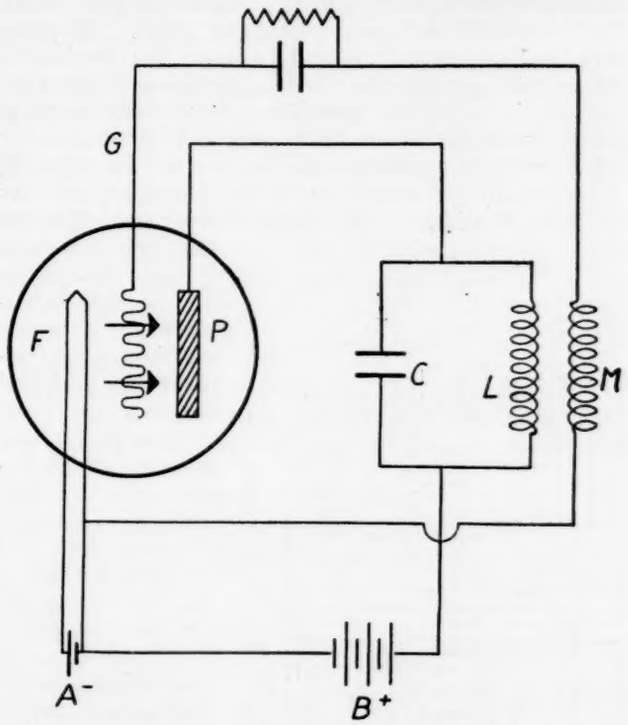


Fig. 2.—Simple oscillator circuit: *F*, filament; *G*, grid; *P*, plate; *C*, condenser; *L*, inductance; *M*, grid coupling inductance; *B*, direct current voltage applied to plate; *A*, current supply to heat filament.

(*b*) *The Oscillator Circuit.*—This consists of a three electrode vacuum tube containing filament, grid and plate connected in a circuit containing a condenser *C* and an inductance *L*, as shown in figure 2. A stream of electrons is drawn by the high voltage from the heated filament to the plate through the grid. The magnitude of this current is controlled by the grid voltage and plate voltage. The closed circuit containing *C* and *L* has the important property of having an alternating current produced within it under the conditions shown. The frequency of the alternating current is determined by the capacity of the con-

denser and the inductance (L) according to the formula $f = \frac{1}{2\pi\sqrt{LC}}$, in which the inductance depends on the size and number of turns of the coil and the capacity (C) depends on the distance between the condenser plates and on their areas and number.[1b] It is to be noted that as the capacity and inductance decrease the frequency increases. With short wave oscillators the capacity and inductance are very small. The plate and filament are made of metal. They are separated by a vacuum and behave as a condenser, which is in parallel with C. Usually this interelectrode capacity is small, but when very short wave radiation (high frequency) is to be produced it is this factor which sets an upper limit to the frequencies that can be produced. In some circuits this is the only capacity in the oscillation circuit. The oscillating current in the LC circuit induces voltage changes in the coupling inductance (M), which are impressed between the grid and the filament and produce fluctuations of the same frequency in the plate current. This phenomenon is called the "grid feed back" and is responsible for the "regeneration" or maintenance of a sustained oscillating current in the LC circuit.

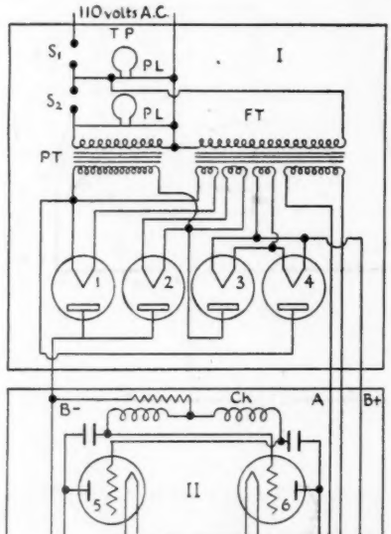


Fig. 3.—Circuit for the production of short wave diathermy current: *I*, power supply; *II*, oscillator circuit; *III*, output circuit; S_1, S_2, switches; *P L*, pilot lamp; *F T*, filament transformer; *P T*, plate transformer; 1, 2, 3, 4, rectifier tubes; 5, 6, oscillator tubes; *C*, *L*, capacity and inductance in main oscillating circuit; *C'*, *L'*, capacity and inductance in external output circuit; *M*, ammeter for measuring current in output circuit; *P*, tissue heated; *B*—, *B*+, direct current voltage to plate filament of oscillator tubes; *A*, low voltage alternating current leads for heating filament of oscillator; *Ch*, choke coil.

(*c*) *The Output Circuit.*—This circuit of the short wave apparatus contains the electrodes or coils which are applied to the patient in addition to a variable condenser, an inductance and a meter. The output circuit is represented on diagram III in figure 3, which shows an assembled short wave diathermy circuit, including the power supply (diagram I) and the oscillator circuit (diagram II). The external circuit containing the patient is inductively coupled to the main oscillating circuit LC. Current in this external circuit is increased or decreased in one of two ways, either by "tuning," i. e. varying the capacity of the output circuit, or by changing the coupling between the output circuit and the main oscillating circuit. By changing the coupling the two inductances L and L' are brought closer together, thus increasing the current in the external circuit.

The assembled circuit is shown in figure 3. The power supply, including transformers and rectifier tubes is shown in diagram I, where the bridge method of rectification, as shown in figure 1, is used. The leads A in figure 3 carry current to heat the filaments of the oscillator tubes 5 and 6. The leads B carry the high voltage rectified current, $B+$ being connected to the plate and $B-$ to the filament of the oscillator tubes. Diagram II of figure 3 shows the main oscillating circuit and its connections. This oscillating circuit is a widely used two tube oscillator type which gives added power and stability, but the principle of operation is the same as the simpler circuit of figure 2. Actually there are many modifications of this typical circuit in use today but the general scheme is the same for all. This type of machine may be used for both long and short wave diathermy current. A similar device has been described by Bishop.[5]

CHARACTERISTICS OF SHORT WAVE DIATHERMY CURRENT

(*a*) *Position of Electrodes.*—When long wave diathermy is used, it is necessary to place the electrodes in contact with the skin. In many treatments this is a satisfactory procedure but in some cases it is unsatisfactory, especially when a large electrode is to be used over some irregular surface in which there are bony projections. With short wave diathermy it is possible to place an insulating pad or to interpose a layer of air between electrode and cutaneous surface, or one may use a coil of fairly rigid insulating cable wrapped around a limb but at some distance from the cutaneous surface. By applying short wave electrodes at a distance, it is possible to heat the desired region without causing irritation of the skin. According to Cumberbatch[6] it is this characteristic of the short wave diathermy that is responsible for the beneficial effects in acute infections of the skin and subcutaneous regions. Krusen[7] states that the difference between the long wave and the short wave diathermy is the convenience of the short wave technic.

The reason contact electrodes must be used with long wave diathermy whereas distant electrodes may be used with the short wave apparatus is the differences in frequency between the two types. Figure 4 represents a conducting tissue between two short wave diathermy electrodes with an air space separating the tissue from the electrodes. The equivalent electrical circuit is also shown. Part of the current passes between the condenser plates as a wattless current indicated by I_1. The conduction current that heats the tissue flows through the resistance R. The system of tissue-air space-electrode at each electrode behaves as a condenser. The impedance of this condenser C_2 is given by the fraction 1/frequency × capacity. The capacity may be increased by bringing the electrode closer to the tissue, since the capacity is inversely proportional to the thickness of the dielectric, in this case air. The impedance to the high frequency current may be reduced by increasing the capacity and increasing the frequency. Hence increasing the frequency allows more current to pass through this condenser and through the tissue. There is some belief that the mechanism of heating and current conduction is different in the two types of diathermy. There is no basis for this belief. The current through tissue consists of oscillating charges. Increasing the frequency causes the ionic

6. Cumberbatch, E. P., and others: Discussion on Short Wave Therapy, Proc. Roy. Soc. Med. **30**: 211 (Jan.) 1937.
7. Krusen, F. H.: The Present Status of Short Wave Diathermy, J. A. M. A. **110**: 1280 (April 16) 1938.

displacement to be less and the rapidity of oscillation greater. If a long wave diathermy machine were connected to short wave electrodes, with an air space between electrodes and tissue, a current would flow but it would be small because of the high impedance of the air space and would be insufficient to cause appreciable heating.

(*b*) *Measurement of Temperature.*—One of the reasons why so little progress has been made in determining the temperature distribution of animals or patients treated with short wave diathermy is that it is not possible to measure the temperature of a heated tissue by a thermocouple or a mercury thermometer during the passage of the current. These metallic temperature measuring devices when placed in a short wave electrical field behave as receiving antennas and foci for the short wave current. In measuring the temperature of a tissue heated by short wave diathermy the customary procedure is to shut off the diathermy current and insert the thermocouple needle into the heated tissue. In the time interval between the shutting off of the current and the final equilibrium deflection of the galvanometer a considerable fall in temperature may occur, especially in a vascular region. Using long wave diathermy to heat a vascular region of the brain of dogs and placing fine wire thermocouples between electrode and brain tissue, we have noted a drop of 3 degrees centigrade in half a minute after the diathermy current was turned off.[8] With long wave diathermy it is possible to measure the temperatures of the heated tissue while the current is flowing. Thermocouples may be used to measure long wave heating effects provided proper precautions are observed as to galvanometer shielding, use of choke coils and position of the thermocouple in the field, according to Stenstrom and Nurnberger [1a] and Hemingway and Hansen.[9]

(*c*) *Measurement of Dosage.*—With long wave diathermy, clinical experience over many years has established definite dosages that are recommended for treatment. These dosages are prescribed in terms of the current density of the smaller diathermy electrode, with 100 milliamperes per square inch of the smaller electrode recommended as the maximum. If the diathermy current passes through a constricted region smaller than the area of the smaller electrode, this dosage must be reduced, as, for example, heating through a knee joint with electrodes above and below the knee.

For many years it was believed that the diathermy current measured by the meter of the long wave machine was not a true heating current. It was believed that a part of the current registered by the ammeter was "wattless" in that it did not produce heat within the tissues. It is theoretically possible that a current passing through the tissues between diathermy electrodes should have a "conduction" component which is responsible for the heating and a "wattless" component which passes across the electrodes as through a condenser, the so-called displacement current. d'Arsonval [10] made measurements of the heat production in solutions heated by long wave diathermy and stated that a large fraction of the total current was wattless. The significance of this observation by d'Arsonval was that it made dosage measurements of long wave diathermy impossible, since a dosage stated in milliamperes per square inch would be useless if a large fraction of the current was wattless. This problem was reinvestigated by Hemingway,[11] and measurements were made of the resistance and phase angle by Hemingway and McClendon [12] of tissues heated by long wave diathermy. It was shown that under clinical conditions the current as registered by the diathermy ammeter was almost entirely conduction current, the wattless component being negligible. In the highest frequencies of the long wave diathermy region, e. g. 2 megacycles per second, the wattless component could be 5 per cent of the total diathermy current.

With short wave diathermy it is not possible to designate dosage in terms of diathermy current which would be applicable to all types of treatment. The reason for this is that as the frequency increases from the long wave range, 0.5-2.0 megacycles per second, to the short wave range, 10-100 megacycles per second, the wattless component of the current increases. The wattless component is increased still more when the electrodes are used at some distance from the skin

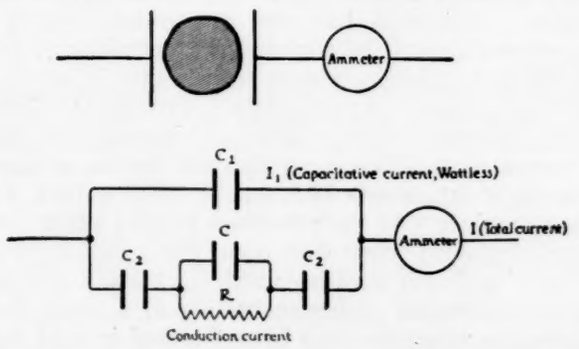


Fig. 4.—Electrical equivalents of tissue between short wave diathermy electrodes.

and varies with shape, size and position of the electrodes. The dosage must be regulated by experience as judged by the sensation of heat in the patient. Once a dosage calibration on this patient's tolerance basis has been established one can assume that for a given position, size and shape of electrode and shape, size and position of the region of the body heated the wattless component remains the same and that the electrical conditions can be repeated.

(*d*) *Temperature and Heat Distribution.*—1. Experiments on Solutions and Dead Tissues: A striking characteristic of short wave electrical fields is that, when the field intensity is kept uniform and electrolytic solutions of various concentrations in test tubes are placed in the field for the same length of time, the rate of heating for the different solutions varies. This effect as described by Hosmer [13] has been verified by others and shown by McLennan and Burton [14] and Pätzold [15] to be a direct consequence of the physical laws governing the heating of electrolytic solutions. According to

8. Stenstrom, K. W., and Nurnberger, Paul: Effect of Diathermy Treatments on Temperature, Arch. Int. Med. **44:** 556 (Oct.) 1929.
9. Hemingway, Allan, and Hansen, C. O.: Temperature Distribution in Local Diathermy Treatments, Radiology **17:** 1258 (Dec.) 1931.
10. d'Arsonval, J. A.: L'échauffement des tissus par les courants de haute frequence, Compt. rend. Acad. d. sc. **185:** 324, 1927.
11. Hemingway, Allan: Thermal Effects of Diathermy. Radiology **14:** 99 (Feb.) 1930.
12. Hemingway, Allan, and McClendon, J. F.: The Measurement of the Heat Production in Diathermy, Physics **4:** 351, 1933.
13. Hosmer, Helen: Heating Effects Observed in High Frequency Fields, Science **68:** 325 (Oct. 5) 1928.
14. McLennan, J. C., and Burton, A. C.: The Heating of Electrolytes in High Frequency Fields, Canad. J. Research **3:** 224 (Sept.) 1930.
15. Pätzold, Johannes: Die Erwarmung der Elektrolyte im hochfrequenten Kondensatorfeld und ihre Bedeutung fur die Medizin, Ztschr. f. Hochfrequentztechnik **36:** 85, 1930.

electromagnetic theory, and supported by experimental observations, the rate of heating of a solution in an electrical field between the electrodes of a short wave diathermy machine depends on the frequency (or wave length) of the alternating electrical field. At a particular frequency, the rate of heating is a maximum. The frequency at which the maximum heating takes place is related to the electrical conductivity and dielectric constant by the formula

$$\text{frequency} = \frac{2 \times \text{specific conductivity}}{\text{dielectric constant}}$$

The various tissues of the human and animal body have specific conductivities which vary widely.[16] Schereschewsky [17] has shown, however, that the dielectric constants of different tissues are practically equal to that of water, 76-78, with the exception of fat, which has a low value of 13.6. The theory would predict that different tissues with these widely varying electrical conductivities would each have a certain specific wavelength at which maximum heating would take place in the high frequency fields. That such maximum heating effects for various tissues do actually occur have been shown by Schereschewsky,[17] McLennan and Burton,[18] Bachem [19] and others. These were dead tissues usually isolated from other tissues in glass containers. There is, however, a considerable lack of agreement among the various investigators as to what wavelength produces a maximum heating effect for a particular tissue. As an example, according to Coulter and Osborne,[20] three different investigators have reported three different wavelengths for the maximum heating of fat, namely 14.5, 3 to 10 and 5 meters. One may conclude that the maximum heating effect for a particular dead tissue does occur for a definite wavelength but that it is variable with the tissue and technic of measurement. Selective heating of a tissue for a particular wavelength has been observed in dead limbs by Schliephake [21] and McLennan and Burton.[18]

Basing these observations on these demonstrations of selective heating of dead tissues, either isolated or in situ, some authors have assumed that this selective heating action applies to tissues in living warm blooded animals. Such assumptions without experimental proof are entirely unwarranted. Those controlled experiments which have been performed for the purpose of investigating this particular problem have shown no selective action, at least in the tissues of human beings.[22]

2. Experiments on Living Animals and Man: As a result of the interesting studies on selective heating as a function of the wavelength of solutions and tissues in vitro, the results of temperature distribution in living tissues becomes a problem of prime importance. The differences between dead excised tissues and living tissues in situ are that: 1. There is in the living body a powerful equalizing action exerted on the tissue temperature by the circulating blood. The importance of this was well demonstrated by Binger and Christie [23] for long wave diathermy. These investigators showed that the circulation through a locally heated region tended to reduce any local rise in temperature. 2. A tissue in situ is in contact with and surrounded by other tissues. These neighboring tissues, which may be good conductors, such as muscle and plasma, tend to exert a "shielding" effect. The heating of a particular tissue such as bone in a living animal is quite a different problem from the heating of bone in a test tube surrounded by glass or air. The measurements of Mortimer [24] have indicated the importance of the equalizing effect of blood flow on temperature of the visceral organs of dogs heated by short wave diathermy. Mortimer and Osborne,[22] Coulter and Carter [22] and Coulter and Osborne [25] have measured the increase in temperature at various sites in human subjects, using short wave diathermy currents of wavelengths from 6 to 24 meters, and have reached the conclusion that there is no specific or selective heating shown that varies with the wavelength. It would seem from their work that one wavelength is as good as another.

CONCLUSION

We wish to emphasize the need for more investigations on the controversial problems, especially the so-called athermic effects. More work is needed on the temperature distributions in various living tissues and the development of better methods of thermometry for temperature measurements during the course of a treatment.

Of particular interest is the development of vacuum tubes capable of producing even shorter radiations than those used in therapy at present. The radiation from these oscillators is of the order of centimeters instead of meters, and such radiation has more pronounced optical properties than the radiation of the short wave field. This 1 to 100 cm. wavelength radiation may be focused [26] and directed along tubes.[27] These properties would seem to indicate that it would be particularly valuable in that the beam could be directed to a desired region. It would be of interest to know the absorption coefficients of this radiation and the extent of their dependence on wavelength and type of tissue. The newer tubes being developed are of the Magnetron type [28] or have resulted from newer designing of the more conventional negative grid tube.[29] It may be that many of the older problems and controversies that have marked the development and final utilization of long wave diathermy and short wave diathermy will reappear when these newer tubes are available for therapy and experiment.

16. Bachem, A.: The Resistance of Tissues for Various Electrical Currents, Arch. Phys. Therapy **11**: 391 (Aug.) 1930. Hemingway, Allan, and McClendon, J. F.: The High Frequency Resistance of Human Tissue, Am. J. Physiol. **102**: 56 (Oct.) 1932.

17. Schereschewsky, J. W.: Heating Effect of Very High Frequency Condenser Fields on Organic Fluids and Tissues, Pub. Health Rep. **48**: 844 (July 21) 1933.

18. McLennan, J. C., and Burton, A. C.: Selective Heating of Short Radio Waves and Its Application to Electrotherapy, Canad. J. Res. **5**: 550 (Nov.) 1931.

19. Bachem, A.: Selective Heat Production by Ultra Short (Hertzian) Waves, Arch. Phys. Therap. **16**: 645 (Nov.) 1935.

20. Coulter, J. S., and Osborne, S. L.: Wavelengths in the Heating of Human Tissues by Short Wave Diathermy, J. A. M. A. **110**: 639 (Feb. 26) 1938.

21. Schliephake, Erwin: Tiefenwirkungen im Organismus durch kurz elektrische Wellen, Ztschr. f. d. ges. exper. Med. **66**: 212, 1929.

22. Mortimer, Bernard, and Osborne, S. L.: Short Wave Diathermy: Some Biologic Observations, J. A. M. A. **104**: 1413 (April 20) 1935. Coulter, J. S., and Carter, H. A.: Heating of Human Tissues by Short Wave Diathermy, ibid. **106**: 2063 (June 13) 1936. Coulter and Osborne.[20]

23. Binger, C. A. L., and Christie, R. V.: General and Local Heat Developed in Living Animal Body by Passage of High Frequency Currents, Proc. Soc. Exper. Biol. & Med. **24**: 677 (April) 1927.

24. Mortimer, Bernard: Experimental Hyperthermia Induced by High Frequency Current, Radiology **16**: 205 (May) 1931.

25. Coulter, J. S., and Osborne, S. L.: Short Wave Diathermy in Heating of Human Tissues, Arch. Phys. Therapy. **17**: 679 (Nov.) 1936; footnote 20.

26. Williams, N. H.: Production and Absorption of Electromagnetic Waves from 3 Cm. to 6 Mm. in Length, J. App. Phys. **8**: 655 (Oct.) 1937.

27. Southworth, G. C.: New Experimental Methods Applicable to Ultra Short Waves, J. App. Phys. **8**: 660 (Oct.) 1937.

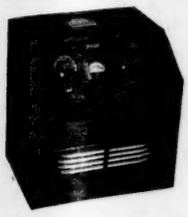
28. Kilgore, G. R.: Magnetron as a High Frequency Generator, J. App. Phys. **86**: 666 (Oct.) 1937. Schereschewsky.[17]

29. Samuel, A. L.: Extending the Frequency Range of the Negative Grid Tube, J. App. Phys. **8**: 677 (Oct.) 1937.

HOGAN ADVANCE MODEL BREVATHERM, MODEL #8640, ACCEPTABLE

Manufacturer: McIntosh Electrical Corporation, 233 North California Avenue, Chicago.

The Hogan Advance Model Brevatherm, Model #8640, is a portable short wave diathermy unit. It may be used for medical diathermy and for minor surgery. It is available with a mobile walnut or ivory finished cabinet, Model #8645. Standard accessories include one set of pad and one of cuff electrodes. Optional accessories consist of inductance cable and electrosurgical instruments.

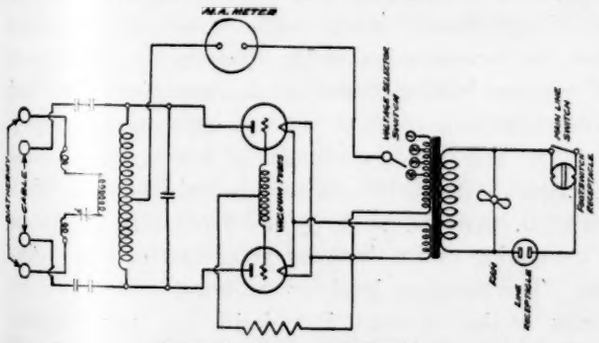


Hogan Advance Model Brevatherm, Model #8640.

The vacuum tubes in a tuned plate, tuned grid, push-pull oscillator circuit generate high frequency energy at a wavelength of approximately 12 meters. The output circuit for the cuff and pad electrodes is inductively coupled and the circuit for the cable is capacitatively coupled to the plate circuits of the oscillator.

The firm claims that the unit has an output of 240 watts as measured by a lamp load, photoelectric cell and wattmeter at a voltage of 116.5. The Council's investigator confirmed these claims. Transformer temperature rise and the temperature rise at various levels within the cabinet after a two hour run at full load were within the limits of safety prescribed by the Council.

The firm submitted thirteen tests, performed by a reliable investigator, as evidence of the unit's ability to produce heat deep in human tissues. The deep muscle temperatures were taken at a depth of about two inches, that is, the full length of the needle was inserted when the size of the leg permitted it. In other cases, the needle was inserted to the bone. A Leeds



Schematic Diagram of Circuit

Northrup Potentiometer was used as well as hypodermic needle thermocouples, in taking the temperatures. All determinations were run first on the right leg, then on the left. In all determinations the time interval between two successive tests on the same leg was never less than one-half hour. The time of application was twenty minutes for each treatment. Room temperature ranged from 75 to 83 F. and the humidity varied from 62 to 70 per cent during the test periods.

Averages for Seven Observations, Cuff Technic

Deep Muscle		Subcutaneous		Skin	
Initial	Final	Initial	Final	Initial	Final
98.1	106.2	94.3	102.7	87.9	92.3

Averages for Six Observations, Coil Technic

Deep Muscle		Subcutaneous		Skin	
Initial	Final	Initial	Final	Initial	Final
98.7	104.9	93.5	103.5	91.8	94.0

Seven tests were made in which the cuff technic was used. The thigh was covered with three thicknesses of flannel and one of toweling, topped with a five-eighths inch strip of felt. The distance between cuffs was from 7 to 9 inches.

Six tests were carried out with the cable technic. A towel was first wrapped around the thigh single thickness and one-half inch felt strips were inserted between the coil and the towel.

The unit was investigated for the Council in a reliable clinic, where it was used for several months for general clinical application. It was reported a satisfactory unit.

In view of the foregoing report, the Council on Physical Therapy voted to accept the Hogan Advance Model Brevatherm, Model #8640, for inclusion in its list of accepted devices.

Council on Foods

ACCEPTED FOODS

THE FOLLOWING PRODUCTS HAVE BEEN ACCEPTED BY THE COUNCIL ON FOODS OF THE AMERICAN MEDICAL ASSOCIATION AND WILL BE LISTED IN THE BOOK OF ACCEPTED FOODS TO BE PUBLISHED.

FRANKLIN C. BING, Secretary.

BAKER'S MODIFIED MILK, POWDERED AND LIQUID FORMS

Manufacturer.—Baker Laboratories, Cleveland.

Description.—Powdered form: A spray-dried homogenized mixture of evaporated skimmed milk, whole milk, lactose, coconut oil, beef fat, dextrose, cod liver oil and gelatin with added wheat germ extract and iron and ammonium citrates, U. S. P.

Evaporated liquid form: An evaporated homogenized mixture of evaporated skimmed milk, whole milk, lactose, coconut oil, beef fat, dextrose, cod liver oil and gelatin with added wheat germ extract and iron and ammonium citrates, U. S. P.

Manufacture.—Powdered form: The milk used is produced by tuberculin tested herds from an accredited area inspected by representatives of the Chicago Board of Health and is regularly inspected at the factory for quality and sanitation. Formula proportions of lactose, dextrose, coconut oil, beef fat, gelatin, cod liver oil, wheat germ extract and iron and ammonium citrates, U. S. P., are added to definite amounts of evaporated skimmed milk and whole milk. The mixture is pasteurized, homogenized, spray dried, packed into cans and hermetically sealed.

Evaporated liquid form: The milk used is the same as for Baker's Modified Milk, Powdered Form. Formula proportions of lactose, dextrose, coconut oil, beef fat, gelatin, cod liver oil, wheat germ extract and iron and ammonium citrates, U. S. P., are added to definite amounts of evaporated skimmed milk and whole milk. The mixture is pasteurized, homogenized, evaporated to a standard total solids content, filled into cans, sealed and heat processed.

Analysis (submitted by manufacturer).—Powdered form: moisture 1.4%, total solids 98.6%, ash 2.9%, fat 24.8%, protein (N × 6.38) 15.0%, carbohydrates (by difference) 55.9%. Liquid form: moisture 75.0%, total solids 25.0%, ash 0.8%, fat 6.4%, protein (N × 6.38) 3.8%, carbohydrates (by difference) 14.0%.

Calories.—Powdered form: 5.06 per gram; 144 per ounce. Liquid form: 1.28 per gram; 36 per ounce.

Vitamins.—Vitamin D: Powdered form, 3.9 U. S. P. units per gram; liquid form, 0.41 U. S. P. units per gram. Both powder and liquid forms supply not less than 400 U. S. P. units of vitamin D per quart, when diluted to "normal" strength as directed on the label.

MRS. PALEY'S BABY FOOD—STRAINED EVAPORATED PRUNES

Manufacturer.—Paley-Sachs Food Company, Houston, Texas.

Description.—Cooked, sieved dried prunes.

Manufacture.—Dried prunes are washed, soaked for twelve hours, precooked in air-tight pressure cookers, automatically pitted, sieved, filled into glass jars, vacuum sealed and heat processed.

Analysis (submitted by manufacturer).—Moisture 68.3%, total solids 31.7%, ash 0.6%, fat (ether extract) 0.1%, protein (N × 6.25) 1.0%, reducing sugars as dextrose 17.1%, sucrose 0.6%, crude fiber 0.6%, total carbohydrates other than crude fiber (by difference) 29.4%, calcium (Ca) 0.026%, phosphorus (P) 0.034%, iron (Fe) 0.002%.

Calories.—1.2 per gram; 34 per ounce.

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SATURDAY, DECEMBER 17, 1938

MODE OF ACTION OF SULFANILAMIDE

Apparently sulfanilamide possesses a specific chemotherapeutic effect on the beta-hemolytic streptococcus; it is of low toxicity, is easily administered, is quickly absorbed and is more effective in vivo than in vitro. The results obtained in the treatment of puerperal sepsis (Colebrook and Kenny) and in hemolytic streptococcus meningitis (Long and Bliss) are sufficiently dramatic to warrant the enthusiasm aroused by this new chemotherapeutic agent. Its administration in man is associated with definite though not necessarily unavoidable or serious hazards. In a recent communication, Long and Bliss [1] analyze toxic manifestations which have occurred during the course of treatment with sulfanilamide in 335 cases at the Johns Hopkins Hospital. The most common toxic effects manifested were dizziness, headache, a loss of ability to concentrate, anorexia, nausea and, in some instances, vomiting. Cyanosis of varying degrees was almost constant. This is said by some observers to be due to sulfhemoglobinemia, by others to methemoglobinemia. Clinical acidosis as evidenced by combination of hypernoia and a lowered carbon dioxide combining power has been noted in 3 per cent of the cases. Jaundice occurred in only one case. Dermatitis occurred in 1 per cent and was apparently associated in one case with photosensitivity of the skin. Simple fever has been the most common toxic reaction noted (6 per cent). An early febrile response was likewise noted in all cases in which dermatitis, acidosis, acute hemolytic anemia or agranulocytosis developed. Anemias of the hemolytic type have occurred quite commonly and in 3 per cent of the cases were of the severe type characterized by a rapid fall in the red blood cell count in the hemoglobin, leukocytosis, reticulocytosis, bilirubinemia, urobilinuria and, in certain instances, porphyrinuria. Other authors have reported cases of agranulocytosis with occasional fatal results. Thus the most serious toxic manifestations are those associated with the blood or hematopoietic system. The mechanism of this type of anemia is not clearly understood, but it would seem to be the result of an idiosyncrasy toward the drug.

Thus in sulfanilamide we have a potent chemotherapeutic agent for combating certain types of invasive bacterial disease. The precise mechanisms of its action on bacteria, as well as its toxic effects, have not been clearly elucidated. Progress is to be anticipated from the experimental studies rather than from the empirical observations of the clinic. A more or less scientific basis for the therapy of sulfanilamide was made possible through the experimental studies of Marshall and his co-workers.[2] They have developed a simple biochemical method for the quantitative demonstration of sulfanilamide in blood and in urine and have pointed out the importance of determining the concentration of the drug in the blood of patients undergoing treatment. Following a single oral dose, the drug is absorbed in about four hours. It is almost entirely excreted in the urine. By repeated dosage of the drug at intervals of four hours an equilibrium can be established between ingestion and elimination and the drug maintained at a definite concentration in the blood and tissues. These observations have been of the greatest importance in establishing a rational basis for therapy in infected human beings. Lockwood [3] demonstrated that the concentration of the drug in the amount of 10 mg. per hundred cubic centimeters of whole blood prevented the multiplication of young virulent streptococci in test tube experiments. Lockwood and his colleagues [4] similarly conclude in this issue of THE JOURNAL that the striking effect of sulfanilamide is a depression of the invasive properties of the organism. The optimum level for treatment in severe cases seems to lie between 5 and 10 mg. per hundred cubic centimeters of blood. Colebrook and his co-workers found sulfanilamide to be bactericidal against hemolytic streptococci in vitro and to a lesser degree in vivo. They did not, however, fail to observe the discrepancy between the striking therapeutic results obtained and the limited bactericidal effect in vitro. They concluded that the effect was the result of the combined bactericidal action of the blood plus that of the body tissues of the animal. Mellon, Cross and Cooper [5] found in their experiments that both sulfanilamide and its derivatives exhibited therapeutic effects in mice against hemolytic streptococcus infections. They found no indication that phagocytosis is a factor in the mechanism of the therapeutic action of these drugs. Likewise they failed to find qualitative changes in the character of the histologic response

1. Long, P. H., and Bliss, Eleanor A.: Toxic Manifestation of Sulfanilamide, Ann. Surg. **108**: 808 (Nov.) 1938.

2. Marshall, E. K.; Emerson, Kendall, Jr., and Cutting, W. C.: Para-Aminobenzenesulfonamide, J. A. M. A. **108**: 953 (March 20) 1937.

3. Lockwood, J. S.: Observations on the Mode of Action of Sulfanilamide and Its Application to Surgical Infection, Ann. Surg. **108**: 801 (Nov.) 1938.

4. Lockwood, John S.; Coburn, Alvin F., and Stokinzer, Herbert E.: Studies on the Mechanism of the Action of Sulfanilamide, this issue, p. 2259.

5. Mellon, R. R.; Cross, Paul, and Cooper, F. B.: Experimental Studies with Sulfanilamide and with Prontosil, J. A. M. A. **108**: 1859 (May 29) 1937.

to the hemolytic streptococcus as the result of the administration of sulfanilamide, Lockwood found that normal serum without leukocytes is just as effective in vitro as a vehicle for the action of sulfanilamide in inhibiting the growth of streptococci. Lockwood found that addition of peptone to the serum in his experiments diminished the ability of sulfanilamide to restrict or to retard the growth of streptococci. He therefore concluded that the drug interferes with the ability of virulent hemolytic streptococci to use serum protein as a food from which to obtain nitrogen.

Most observers agree that the addition of sulfanilamide to nutrient broth or human serum slows the rate of multiplication but does not lead to the destruction of beta-hemolytic streptococci. The action of the drug, however, is not completely explained by this bacteriostatic influence, since it was proved that it enhances the bactericidal powers of human blood in infected patients. Lyons [6] found that sulfanilamide rendered human virulent strains of hemolytic streptococci more susceptible to the bactericidal action of human blood and that this effect is reversible on withdrawal of the drug. He found that in certain types of sustained hemolytic streptococcus bacteremias it was necessary to add an antibacterial antibody to sulfanilamide in order to obtain a therapeutic effect. The effective therapy for this type of infection should consist of sulfanilamide and the intravenous injection of specific antibacterial antibody by the immunotransfusion technic. He concludes that sulfanilamide induces a physiochemical alteration in the antigenic structure of hemolytic streptococci which decreases the invasive capacity or virulence of the bacteria.

6. Lyons, Champ, with the Technical Assistance of Mangiaracine, Anita: The Effect of Sulfanilamide upon Human Virulent Hemolytic Streptococci, Ann. Surg. **108**: 813 (Nov.) 1938.

FORMATION OF MILK PROTEINS

The phenomenon of lactation is of perennial interest to the physiologist, biologic chemist and pediatrician. Not only is the period of preparation an illustration of fine endocrine coordination and balance but the actual production of milk presents an opportunity to study metabolism taking place at an unusually rapid rate. The turnover of materials incident to the elaboration of large quantities of milk may present astounding values. Some dairy cows have made records of 100 pounds of milk a day; this yield means a large consumption of feed and water. It means the annual loss by way of the mammary glands of some 150 pounds of ash, of 25 pounds of calcium, of ten times the organic matter contained in the cow's body and of more than 1,000 pounds of protein.

The product of the mammary gland for several days post partum is unusually rich in protein. This secretion, called colostrum, contains in the case of the cow about 17 per cent of protein, a large proportion of which is a globulin identical with serum globulin. Ordinarily globulin accounts for a small part of the total protein of milk, so that this high concentration in colostrum is striking and suggestive. It has been shown that this protein, after having been consumed by the newborn calf, passes unchanged through the intestinal wall into the blood, thus providing serum globulin for the calf whose blood during early life is essentially devoid of this immunologically important constituent.

The origin of the milk proteins was early studied by Cary,[1] who reported a withdrawal of amino acids from the blood as it passed through the mammary gland. He concluded that the proteins of milk arose from these amino acids taken from the blood. An analysis of the blood of lactating women, however, did not show any deviation from the normal in the level of amino acids.[2] Other reports showed that the nonprotein nitrogenous constituents of milk and those of blood were similar in concentration, and later identical values for urea were found in these two body fluids. That the protein of the gland itself is not changed in quantity has recently been shown by Jackson and Gortner;[3] this cannot be seriously considered as a source of milk proteins. A reexamination of the quantitative relationship between the amino acids withdrawn by the mammary gland and the milk protein formed by this gland has shown that not more than from 30 to 40 per cent of the total milk protein can be accounted for by the amino acids removed from the blood if all the amino acids are changed to protein.[4] A more recent study has indicated other sources of the milk protein; on the basis of extensive comparisons of the analysis of arterial blood with that of mammary venous blood, Graham, Peterson and Houchin [5] have concluded that serum globulin is removed by the mammary glands during active secretion. Furthermore, unidentified nonprotein nitrogenous compounds as well as amino acids pass from the blood into the glands at this time. The conclusion warranted by the current evidence is that the constituents of the blood from which the milk proteins can be synthesized by the mammary glands are amino acids, serum globulin and certain nitrogenous compounds of unknown nature.

The process of elaboration of milk is accompanied by intense nitrogen metabolism of another sort, which may or may not be concerned with protein synthesis. The gland forms urea in the course of its activity, raising the concentration of this substance in the mammary venous blood over that in the arterial blood.[6] Nursing or milking accentuates the production of urea by the glands. Shaw and Petersen [7] have shown that the active glands contain arginase, whereas the quiescent glands

1. Cary, C. A.: J. Biol. Chem. **43**: 477 (Sept.) 1920.
2. Harding, V. J., and Downs, C. E.: J. Biol. Chem. **84**: 335 (Oct.) 1929.
3. Jackson, S. M., and Gortner, R. A.: J. Biol. Chem. **123**: 719 (May) 1938.
4. Shaw, J. C., and Petersen, W. E.: Proc. Soc. Exper. Biol. & Med. **38**: 632 (June) 1938.
5. Graham, W. R., Jr.; Peterson, V. E.; Houchin, O. B., and Turner, C. W.: J. Biol. Chem. **122**: 275 (Jan.) 1938.
6. Graham, W. R., Jr.; Houchin, O. B., and Turner, C. W.: J. Biol. Chem. **120**: 29 (Aug.) 1937.
7. Shaw, J. C., and Petersen, W. E.: Proc. Soc. Exper. Biol. & Med. **38**: 631 (June) 1938.

do not. This enzyme forms urea from the amino acid arginine and doubtless accounts for some of the urea which the gland loses to the blood. Whether the urea mechanism is a device to remove extra amino acids or is involved in the production of milk protein remains to be determined. Certain it is that recent investigation of the metabolism of nitrogen incident to the production of milk has brought us nearer to an understanding of the synthesis of proteins by the mammary gland.

Current Comment

SALIVARY INFLUENCE ON GALVANISM

Much has been written indicating that the electrical potential differences between dissimilar metals may produce damage to the mouth when such metals are used in dental restorations. Solomon and his co-workers [1] have recently reported a series of ingenious experiments to determine whether differences of potential actually exist between dental metals when saliva is the electrolyte. While the initial currents with saliva as the electrolyte are greater than currents with an artificial saliva, the final values are lower, showing that some action other than polarization is occurring, namely film formation. They concluded therefore that electric current is not normally flowing in the mouth containing dissimilar metal restorations. Although they do not maintain that electrical action resulting in damage to the soft tissues cannot exist in a mouth, the so-called protective mechanisms must be removed in order to permit current to flow. These investigators contend that there is no connection between the current readings obtained by placing a meter between metallic restorations in the mouth and damage to tissue.

GERMICIDAL ACTION OF PROSTATIC FLUID

The demonstration by Youmans and his colleagues [1] of Northwestern University that prostatic fluid contains a bactericidal substance more powerful than blood serum is a belated confirmation of a generally accepted theory of genito-urinary immunity. The Northwestern University bacteriologists obtained prostatic fluid aseptically from dogs by the Farrell-Lyman technic, pilocarpine being used as the secretory stimulant. They tested its germicidal action against such micro-organisms as Bacillus coli, Staphylococcus aureus, hemolytic streptococci, Streptococcus viridans and the gonococcus. When Bacillus coli, Staphylococcus aureus or hemolytic streptococci were added to the undiluted prostatic fluid they found that the number of viable micro-organisms was reduced fully 95 per cent by the end of two hours. Within four to twenty-four hours all mixtures became sterile. This germicidal action was more rapid and complete than that of the blood serum of the same donors. Tests with the gonococcus showed a somewhat slower rate of bacteriolysis, but all gonococcus mixtures became sterile by the end of twenty-four hours. The bactericidal power of canine prostatic fluid is but slightly reduced by dilution even with as much as twenty volumes of distilled water. The germicidal power, however, is reduced 50 per cent by heating the fluid to 55 C. for thirty minutes and is completely destroyed at 60 C. for thirty minutes. The bactericidal substance in prostatic fluid, therefore, is not identical with the lysozyme of tears or saliva, which resists heating to 75 C. for thirty minutes. Since the prostatic fluid will not activate hemolytic amboceptor it contains no demonstrable serum complement. Nor is the action of the germicidal factor increased by the addition of complement. Whether or not prostatic bacteriolysin is bound or inhibited in the presence of whole blood or pus has not yet been determined.

SULFANILAMIDE AND BACTERIOSTASIS

In a recent report on the mechanism of action of sulfanilamide on bacterial infections, Osgood and Powell [1] found that sulfanilamide in concentrations of 1:1,000 or less did not inactivate in vitro significant amounts of the hemotoxins of the beta hemolytic streptococcus, hemolytic Staphylococcus aureus, Clostridium oedematis-maligni, Clostridium tetani or Bacillus perfringens. Neither did sulfanilamide therapy significantly affect the course of intoxication in guinea pigs injected with as little as 1 minimal lethal dose of diphtheric or tetanus toxin. The results of these experiments, therefore, fail to support, although they do not disprove, the earlier experiments with cultures of human bone marrow reported by the senior author indicating that sulfanilamide in some manner interferes with the production of the toxins responsible for the virulence of the organism and for its resistance to small amounts of bacteriocidins. Maegraith and Vollum [2] have recently investigated the bacteriostatic properties of three sulfanilamide derivatives using Staphylococcus viridans and Staphylococcus aureus, examined by the slide method of Wright, modified by Fleming. This technic was also used in cases of Neisseria gonorrhoeae and Neisseria meningitidis. All three derivatives apparently inhibited the growth of Streptococcus viridans in a dilution of 1:2,000 in the presence of defibrinated human blood but none of them were effective in the absence of leukocytes. None exhibited any bacteriostatic effects on Staphylococcus aureus; all three retarded the growth of Neisseria gonorrhoeae and Neisseria meningitidis. The bacteriostatic effect was dependent on the presence of leukocytes, which was in agreement with the observations previously reported by Fleming. The consensus at present is therefore that sulfanilamide and some of its derivatives exert a bacteriostatic effect in different degrees depending on the type of organism and the nature of the derivative but that the presence of leukocytes and probably some other factors are necessary for effective action.

1. Solomon, H. A.; Reinhard, M. C., and Goltz, Hilda Lee: Salivary Influence on Galvanism, Dental Items of Interest **60**: 1047 (Nov.) 1938.

1. Youmans, Guy P.; Liebling, Joseph, and Lyman, R. W.: J. Infect. Dis. **63**: 117 (July-Aug.) 1938.

1. Osgood, E. E., and Powell, H. M.: Failure of Sulfanilamide to Inactivate Preformed Hemotoxins, Diphtheric Toxin or Tetanal Toxin, Proc. Soc. Exper. Biol. & Med. **39**: 37 (Oct.) 1938.

2. Maegraith, B. G., and Vollum, R. L.: The Bacteriostatic Effects of Sulphonamide-P, Soluseptasine, and M & B 693, Brit. M. J. **2**: 985 (Nov. 12) 1938.

ORGANIZATION SECTION

AMERICAN MEDICAL ASSOCIATION STUDY OF MEDICAL CARE

Sullivan County, Tennessee

Sullivan County, Tenn., with a population of about 51,000, is located in the northeastern part of the state. The gainfully employed persons are about equally divided in agriculture and industry. The two industrial centers, Kingsport and Bristol, have a population of approximately 12,000 each.

The forty-six physicians in active practice in the county are located so that no person is more than 7 miles from the nearest physician. There are twenty practicing dentists, ten private duty nurses and ten public health nurses. There are two nonprofit general hospitals with a total of 111 beds. During 1937 the average bed occupancy was 41 per cent. Daily rates range from $2.50 to $6. In addition to two clinics operated by the hospitals there are five clinics maintained by the health departments and eight by welfare and relief agencies. Of the fifteen clinics, three provide general medical and surgical services and two are dental clinics. The rest provide limited special services but as a group they offer all types of medical and dental services.

Record for One Week of Free Medical Services Furnished by Physicians

1. Number of forms received		9
General practice	4	
Surgery	2	
Internal medicine	1	
Eye, ear, nose and throat	2	
2. Total number of persons who received any form of medical services in home or office		820
3. Total number of persons who were served without charge		141
4. Total number of persons referred to some other source for free medical care		23
5. Free surgical operations		13

The hospital provided 21,653 days of hospital care. Of this total, free patients received 2,716 days. In determining a patient's ability to pay, the hospital investigates his financial status and checks with the relief agency to see whether the patient is entitled to governmental aid.

Medical care for the indigents is provided by the Welfare Department, Salvation Army, Community Chest, Red Cross and Parrish Vance Foundation. These various organizations make their own investigations in determining the indigence of a person. If a person is found to be unable to pay for necessary medical care he is provided with free medical services at the various clinics. In addition to this public health nurses made 17,240 visits to patients at no charge, and the pharmacists provided 1,195 free prescriptions. The board of education provides free examinations and medical treatment for public school children.

Physicians and dentists reported that during 1937 there were thirty-two instances in which persons could not obtain medical care and the reasons given were listed as follows:

1. Lack of first class hospital.
2. Inability of patient to pay.
3. Refusal of physicians to take maternity cases in which antepartum care has not been given.
4. Refusal of patient to take advantage of services available.
5. Lack of free hospital service.

The welfare and relief agencies stated, however, that there were no cases of persons needing medical care who were not provided with the necessary services.

The amount of free medical care furnished by physicians may be estimated from the accompanying report, which is a summary of the data obtained from Form 1F.

Physicians in private practice through the health department and welfare agencies performed preventive medical services. Of the total number of children who entered school for the first time in 1937, 75 per cent were successfully vaccinated against smallpox.

In Kingsport and Bristol the larger business organizations provide industrial health services to their employees. The business men's clubs of these two cities are helpful in providing medical care, eye examinations and glasses when needed and food to needy children. In some cases these medical services are obtained for adults as well as for children.

The following comments and suggestions accompanied the county medical society summary sheet:

SUGGESTIONS FOR SUPPLYING MEDICAL NEEDS

Comments:

1. For fifteen years ample medical services have been available for all who applied.
2. Any lack of medical care in this community is due to failure of patients to avail themselves of the existent facilities.
3. A large group of diseases are nutritional rather than medical problems.
4. Many people who cannot afford adequate medical care will not go to a free clinic because of the 'stigma' attached to so doing.
5. There is a need for more adequate medical service to the indigent.

Suggestions:

1. Some free hospital beds for the indigent should be provided.
2. Complete care of cases should be relegated to the general practitioners. All clinic work, care of the indigent, and so on, should be done by physicians paid minimum fees for their service by relief and health agencies.
3. The most important needs in this locality are:
(*a*) Free choice of physician.
(*b*) Staff organization to improve hospital service.
(*c*) Hospitalization for very low income groups.
(*d*) A more efficient system of eliminating from charity those who are able to pay at least a small fee.
(*e*) More and better outpatient clinics.
(*f*) Organized follow-up clinics.
(*g*) Education of the public with regard to the value of medical attention early in an illness.

The county medical society makes the following conclusions and recommendations based on the experience of its members in making this study:

CONCLUSIONS AND RECOMMENDATIONS

It is our opinion, drawn from this study, that the medical care of the indigent is a community problem and an economic burden that has been borne too long by the physicians. The most equitable distribution of the costs of such care should be through tax support, and that cost should include anything

necessary for the care of the medically indigent person who is ill or injured, be it hospitalization, nursing or anything else that would make up an efficient medical regimen for that individual.

We advocate the free choice of physicians for the care of the medically indigent, and payment of those physicians for services rendered through the local governing unit. We have no desire to pass upon indigence because we feel that, while we have considerable information about certain families, owing to the nature of our profession, yet declaring a person medically indigent is the work of people trained for that purpose.

We disapprove of the employment of county or city physicians for the care of the poor, at least as far as it applies or is applied in Sullivan County. We find that no investigation is made of the indigent, but those who have been on the indigent roll for some time call the city or county physician to take care of their injuries or illnesses.

Owing to the past subsidization of our county health work by the Commonwealth Fund, we have a county health unit that is probably not only second to none in the state but ranks with the best of the country. It is exceptionally well housed in a building erected by the Commonwealth Fund.

The medical care of the prisoners at the county jail cannot be accomplished efficiently under the crowded, poor sanitary conditions existing in that institution. The same applies with regard to the medical care of people housed at the poor farm. The work in these two institutions is done under the supervision of county physicians who are inadequately paid for inadequate service. They have no facilities with which to do good work, and we cannot be proud of it.

The hospital service plan at Kingsport has the approval of the American Hospital Association and is working out very nicely. The hospital facilities in both Kingsport and Bristol are excellent; but this also, as far as housing and equipment are concerned, is due to subsidies by an outside agency, the Commonwealth Fund.

There is no sanatorium care provided for the patients with tuberculosis in East Tennessee. The facilities for the care of the insane are on a par with that which is happening in a large percentage of the states of the Union, in that a commitment to the state hospital automatically turns the patient over to the sheriff, and the insane person is lodged in jail until he can be transported to an overcrowded state institution.

As already stated, we do not wish to pass upon indigence, but we wish it to be well done; and it was found during the depression of the early thirties that as a general rule counties did not have an efficient poor relief organization. We would therefore recommend that the federal government be requested by the American Medical Association to cooperate through the state government with county authorities, in subsidy funds and poor relief organization policy. Under this plan, both state and county, in order to qualify for such subsidy from the federal government, had to arrange for a businesslike efficient investigation and purchasing system in their relief work. This system, with a personnel properly selected by local county officials, was efficient. We know that the people who were doing that relief work in this county during the depression years did a good, conscientious, nonpolitical job.

The medical care of the indigent should be under the supervision of, and should be controlled solely by, physicians. The indigent person should have a free choice of physician from the list of the physicians in the county or group of counties who are willing to do this work at fees agreed on between the governing board of the county and the county medical society.

Bills for services rendered would be audited by a committee of physicians appointed by the county, and this committee should be composed of men who are willing to disagree and openly criticize any physician who attempted to impose on the system and make his relief work a "racket."

We feel definitely that there is going to be more socialization of medicine and that unless the American Medical Association and the Tennessee State Medical Association plan to meet the needs of the group who possibly cannot secure medical care and who are the group referred to by the Interdepartmental Committee in Washington as one third of the population, a system of state medicine will be crammed down our throats, and we shall have no alternative but to accept it.

We submit this plan as one that we believe will meet the need of the times and take away from the complete state medicine advocates their only definite evidence of the lack of distribution of medical care.

GRADUATE MEDICAL EDUCATION IN MISSOURI

Report of Recent Progress

At the last annual meeting of the Missouri State Medical Association, the Committee on Postgraduate Course recommended to the house of delegates that a correlating committee be formed of chairmen of the various state society committees concerned with professional and lay education.[1] October 13 the Postgraduate Correlating Committee was effected, with Dr. C. H. Neilson, who has been active in arranging postgraduate courses for several years, as chairman of the newly formed correlating committee and representatives from the committees on cancer, conservation of eyesight, fractures, health and public instruction, maternal welfare, medical economics, mental health, publication, physical therapy and the control of syphilis. Dr. John W. Williams, assistant health commissioner, also attended this meeting.

In the future the educational activities of these committees of the state association will be reviewed by the correlating committee, thus avoiding duplication of effort and insuring a well planned, comprehensive and continuous program of professional and lay instruction. Particular stress is to be given to the recording and publication of attendance at both scientific and lay meetings.

The newly formed correlating committee will strive to demonstrate to the public that individual practicing physicians are being thoroughly instructed and informed on the recent advances in medical science and practice under the present system of individual care. The plan of professional and lay education on preventive medicine of the Indiana State Medical Association, approved by the House of Delegates of the American Medical Association at the San Francisco session, forms the principles on which the Missouri association's postgraduate correlating committee will function. These are:

1. The selection of a specific disease or health problem of major importance for discussion in the state association's journal and in each county medical society. For each successive month, beginning in December, the following subjects have been chosen: pneumonia, highway accidents, syphilis, maternal and infant care and diphtheria. It is suggested that each component society select speakers from its own membership, whenever possible, to discuss current topics. Articles published in the journal should be of considerable assistance. Smaller county societies might arrange to meet jointly when circumstances permit.

2. Continued cooperation with the state board of health in the statewide program of lectures in obstetrics and pediatrics is strongly urged. Likewise, in the discussions of syphilis, the profession should be completely informed of the board's plan for the control and treatment of this disease.

3. The correlating committee does not propose to interfere with the activities of individual committees. As in the past,

1. Association's Postgraduate and Health Education Activities Correlated, J. Missouri M. A. **35**: 454 (Nov.) 1938.

the office of the state association will continue to be the clearing house for all committee activity. The number of physicians attending scientific sessions and the lay interest in health programs is to be reported routinely by the secretary of each component society to state association's office.

4. It has become a policy for the speaker designated for professional audiences to address lay groups as well when so requested by the local society.

5. Publicity on preventive health educational activities will be directed by the postgraduate committee in cooperation with the state association's office and component societies. Members of the committee on postgraduate course "believe that through such correlated activity we can successfully demonstrate to the public that individual practitioners of medicine are being thoroughly instructed and informed on the latest methods of medical progress. . . ."

OFFICIAL NOTES

WITNESSES BEFORE THE SPECIAL GRAND JURY IN WASHINGTON

The following additional witnesses are reported to have appeared before the Special Grand Jury in Washington, D. C.: Dr. John E. Rueth and Dr. Adam L. Curtin, both of Milwaukee.

RADIO BROADCASTS

The fourth series of programs broadcast in dramatic form portraying fictitious but typical incidents of significance in relation to health by the American Medical Association and the National Broadcasting Company, entitled "Your Health," began Wednesday October 19 and will run consecutively for thirty-six weeks. The program is broadcast each Wednesday over the blue network of the National Broadcasting Company at 2 p. m. eastern standard time (1 p. m. central standard time, 12 noon mountain time, 11 a. m. Pacific time).[1]

These programs are broadcast on what is known in radio as a sustaining basis; that is, the time is furnished gratis by the radio network and local stations and no revenue is derived from the programs. Therefore, local stations may or may not take the program, at their discretion, except those stations which are owned and operated by the National Broadcasting Company.

The next three programs to be broadcast, together with their dates and their topics, are as follows:

December 21. Hidden Treasures in Foods.
December 28. Good Milk, Good for You.
January 4. Fool's Gold.

1. Owing to program conflicts, there will be no Chicago broadcast of the network program. Instead, a recording of the program will be broadcast over station WENR at 8 p. m. each Wednesday. This recording will be an identical rebroadcast of the network program broadcast earlier the same day.

SPECIAL BROADCAST ON INFANTILE PARALYSIS

The American Medical Association and the National Broadcasting Company, in cooperation with the National Foundation for Infantile Paralysis and the Committee for the Celebration of the President's Birthday, will broadcast a special program on infantile paralysis over the red network of the National Broadcasting Company December 19 at 11:30 p. m. to midnight, eastern standard time (10:30 central standard time, 9:30 mountain time and 8:30 Pacific time).

This will be a dramatized program, with music, along the same general lines as the regularly weekly programs in the Your Health series. The program will be conducted by Dr. W. W. Bauer and the principal speaker will be Dr. Morris Fishbein.

WOMAN'S AUXILIARY

Georgia

Dr. Grady N. Coker, president of the Medical Association of Georgia, spoke on "Our Problems" at a recent meeting of the auxiliary to the First District Medical Society. Dr. W. H. Myers, president-elect, spoke on "What Is Happening in the Practice of Medicine."

The auxiliary to the Third District Medical Society held a joint meeting with the society in Eastman recently. Speakers and their subjects were as follows: Mrs. Warren A. Coleman, president of the auxiliary to the Medical Association of Georgia, "Auxiliary Activities for 1938-1939"; Mrs. Eustance Allen, president-elect, "Organization"; Mrs. John Persall, "The Jane Todd Crawford Memorial," and Mrs. R. L. Cater, "Research in the Romance of Medicine."

Iowa

The auxiliary to the Dallas-Guthrie Medical Society met at Panora October 20. Mrs. Dean W. Harman, president of the Iowa Auxiliary, gave the four auxiliary objectives for the year: 1. Extend aim of medical society to all organizations interested in health. 2. Assist in entertainment work at state meetings. 3. Promote friendship among families of physicians. 4. Continue to cooperate with medical societies in all tasks for which they ask our help.

New Jersey

The auxiliary to the Atlantic County Medical Society met October 4 at the Ambassador Hotel, Atlantic City. Dr. Hilton S. Read was speaker. Mrs. Andrew Smith, president, announced the essay contest sponsored by the auxiliary for children of the seventh and eighth grades of the public schools of Atlantic County.

The auxiliary to the Bergen County Medical Society met at Teaneck October 11. At the request of the society, three needy physicians will be assisted from the philanthropic fund of the auxiliary.

The auxiliary to the Hudson County Medical Society met in Jersey City October 3. Mr. David Armstrong, professor of English in the Emerson High School, Union City, reviewed the Biography of Madame Curie, written by her daughter.

The auxiliary to the Middlesex County Medical Society met at Perth Amboy October 27. Mrs. Don Epler, president of the state auxiliary, was guest of honor. Dr. Rita Finkler of Newark, director of the biologic laboratory at the endocrine clinic, Beth Israel Hospital, Newark, spoke on "Recent Advances in Endocrinology."

Dr. Sigurd Johnsen of Passaic spoke on "Socialized Medicine" at the meeting of the auxiliary to the Passaic County Medical Society October 10.

Oklahoma

The auxiliary to the Woodward County Medical Society, comprising the five counties of Beaver, Harper, Ellis, Dewey and Woodward, hold joint meetings alternate months. October 15, Dr. Louis H. Ritzhaupt spoke on "Socialized Medicine." The project for the year is to organize a speakers' bureau and to furnish programs on public health for lay groups.

The auxiliary to the Pontotoc County Medical Society met in Ada October 19. Mrs. C. F. Needham gave a talk on "Public Relations." The auxiliary is cooperating with the American Association of University Women in federal nursery work and during the past month supplied cod liver oil, foodstuffs and toilet articles for thirty needy children.

The auxiliary to the Tulsa County Medical Society held a tea in Tulsa October 4 with ninety-two members present. Copies of "On the Witness Stand," a booklet on socialized medicine, was distributed.

Tennessee

The Woman's Auxiliary to the Nashville Academy of Medicine and the Davidson County Medical Society gave a dinner October 24 in honor of Dr. Harrison H. Shoulders, Nashville, Speaker of the House of Delegates of the American Medical Association, and Mrs. Shoulders.

Wisconsin

The auxiliary to the Dane County Medical Society met in Madison October 12. Mr. J. G. Crownhart, secretary of the Wisconsin Medical Society, spoke on "Looking at Sickness Care in Europe." Mr. Crownhart was speaker also at the meeting of the Milwaukee County auxiliary October 14 on the subject "Current Medical Problems."

The auxiliary to the Sheboygan County Medical Society assisted the society and the Crippled Children's Division of the Department of Public Instruction at the orthopedic clinic held in Sheboygan September 26.

MEDICAL ECONOMIC ABSTRACTS

DIPHTHERIA PREVENTION IN ENGLAND

A vivid comparison of the preventive measures taken against diphtheria and the results of such measures in the United States and Great Britain is found in the following extract from the Annual Report of the Chief Medical Officer of the Ministry of Health for the year 1937 "On the State of the Public Health," London, 1938, pages 53-55:

In 1937, 61,339 cases of diphtheria were notified as compared with 57,795 in 1936 and 65,084 in 1935. The fatal cases numbered 2,963, giving the fatality rate of 4.8 per cent as compared with 5.3 per cent and 5.4 per cent in 1936 and 1935 respectively. In diphtheria we appear to have reached a position of stability so far as incidence is concerned within the limits of what may be regarded as normal fluctuation, and it is doubtful whether any marked diminution of incidence can be expected by procedure along the old lines of "notification, removal and disinfection."

Approximately 90 per cent of cases of diphtheria occur under the age of 15 years. By that time the great majority of individuals have become immunized by the subclinical infection. This is a measure of the amount of natural subinfection which is constantly taking place. The acquisition of immunity by natural means postulates a diphtheritic environment. It is a lengthy process and is obtained at the expense of a number of clinical cases, and possibly of deaths, whereas artificial immunity if carefully conducted by experts is without these risks and can be acquired in as many months as the natural process takes years. A clear indication would appear to be to induce a wider adoption of artificial immunization, such as has been practiced in certain cities of the United States of America and in Canada with extraordinary success.

RESULTS OF IMMUNIZATION IN NORTH AMERICA

In New York immunization against diphtheria has been a practice for about twenty years. An intensive campaign began in 1929 and by the middle of 1935 more than 1,110,000 children under the age of 15 years were immunized in addition to those protected in previous years.

Before 1929 comparatively little attention has been paid to children of preschool age on whom, as previously pointed out,[1] the maximum incidence and fatality falls, but in 1929 in New York special attention was paid to the children, and the total number of immunized persons rose from 212,000 in 1929 to 1,114,325 in 1935. Of this last number 650,000 were under the age of 6 years and it is estimated that between 65 and 70 per cent of them had been protected. There resulted a reduction in diphtheria incidence from 8,548 cases in 1929 to 1,143 in 1936. That is to say, the incidence in the latter year was about one-eighth what it had been in the former. During the same period the deaths diminished from 463 to thirty-five. The later figures represent a reduction in the diphtheria death rate in the age period 1 to 15 from 27.4 to 2.1 per hundred thousand. The corresponding figures for England and Wales are 32.8 and 31.8 respectively.

In Montreal, among a population of 657,000 in 1928 when immunization was commenced, there were 1,632 cases and 157 deaths from diphtheria. Both incidence and mortality fell *pari passu* with immunization until in 1935 there were 183 cases and twenty-one deaths, approximately one tenth of the figures recorded in 1927. As in New York, a particular effort to secure the protection of young children was made and it was calculated that by the end of 1935 over 50 per cent of the child population under the age of 12 was immunized. Among other smaller cities of Canada showing an almost similar record are Toronto (650,000), Hamilton (150,000), where there has been no case of diphtheria notified since 1933 and no death since 1930, Brantford (31,382) and St. Catherines, Ont. (27,000). Of Brantford it is said that no child has suffered from diphtheria there since 1930, and from that date no resident of St. Catherines has died from diphtheria.[2]

These results have been achieved only by intensive propaganda on the part of local authorities, assisted in some degree by insurance interests, and it is, of course, necessary to ensure that the immune population thus obtained is not unduly dilated with nonimmunes in the persons of recently born infants, for, as Dr. Graham Forbes[3] recently observed, the further success of immunization must be dependent on the respective campaigns being continuous and unremitting in order to keep the protection rate at least equal to one-half the number of births each year.

It is now six years since the minister issued his memorandum on "The Production of Artificial Immunity against Diphtheria" and drew the attention of local authorities to the advantages of this process, at the same time expressing the opinion that the public should be made aware of them, and, where practicable, parents and guardians of children over 1 year of age should be offered the necessary facilities for protection. A survey of the annual reports for 1936 of medical officers of health, the last complete available information, shows that local authorities generally are well acquainted with the memorandum and continuous if slow progress is being made, particularly in some of the larger provincial cities, although none of them have yet succeeded in immunizing the 50 to 60 per cent of the child population which is necessary before the incidence of the disease is affected. Chester, with an estimated number of 45 per cent, is probably the best immunized town in the country; then follow in close order Birmingham, Walsall, Worcester, Leeds, Manchester and Chatham, all of which are in the neighborhood of from 35 to 40 per cent. Other towns with more than 30 per cent are Wood Green, Wakefield, Salford, Blackburn, Swindon, Cardiff and Acton. London (all the metropolitan boroughs combined) appears very low in the list, with an estimated number of 5.3 per cent of her child population immunized.

It may be said in conclusion that artificial immunization against diphtheria as done in the United States and Canada has been attended by extraordinarily good results. This work has to be persisted in over a long period of time before the necessary number of immunes are obtained to affect the incidence of the disease. It is unfortunate that the exact technic, preparation of vaccine and method of administration are still matters of medical controversy. It is probable that the lack of a general standard has militated against the more general adoption of antidiphtheritic immunization in this country. It is a form of preventive treatment which in the future may succeed in eradicating diphtheria from our midst and thus save countless lives. It is desirable that medical practitioners should

1. Annual Report of Chief Medical Officer of Ministry of Health for 1934, p. 26.

2. Fitzgerald, J. G.; Fraser, D. T.; McKinnon, N. E., and Ross, Mary A.: Lancet **1**: 391 (Feb. 12) 1938.

3. Forbes, J. Graham: Brit. M. J. **2**: 1209 (Dec. 18) 1937.

acquaint themselves with the minister's memorandum and, if possible, gain practical experience at a clinic where immunization is done, in order that they may be familiar with the method when called on to apply it. The medical officer of health of the county or county borough concerned is usually able to make the necessary arrangements for medical practitioners to acquire experience in the technic employed in Schick testing and immunization, and applications should be made to him.

INFANT MORTALITY IN GERMANY

When so much is being said about comparative infant mortality statistics, it is worth while to look at some of the facts. Germany has had sickness insurance longer than any other nation in the world. In the *Deutsches Aerzteblatt* (**68**:681 [Oct. 1] 1938) Hans Klepp reports on "The Struggle Against Infant Mortality" and gives a table showing the course of infant mortality during the present century, from which the following figures are taken:

Death Rate per Thousand Live Births During the First Year

Year	Male	Female	Both
1901	223	190	207
1905	222	188	205
1910	176	147	162
1913	164	137	151
1914	177	149	164
1918	172	143	158
1919	158	131	145
1923	144	118	131
1928	99	79	89
1929	107	86	97
1932	87	71	79
1933	85	68	77
1935	77	60	69

The Bureau of the Census, Department of Commerce, has also issued a summary of the changes in infant mortality in the registration area since 1915 (Vital Statistics—Special Reports 5:47 [March 1] 1938). Every state that is in any way comparable as to climate and racial uniformity with Germany shows a lower infant mortality rate. Of eleven northern states that have been in the registration area since 1920, the range of the infant death rate per thousand in 1935 is between 41.2 for Oregon and 53.9 for New Hampshire.

PWA HOSPITAL CONSTRUCTION

According to a report on "Allotments for Hospital Construction" by the Federal Emergency Administration of Public Works, Projects Division, Research Section, Dec. 2, 1936, and supplemental report as of Jan. 15, 1938, the total estimated cost of constructing and equipping 1,161 hospital buildings was $194,567,038. Nine hundred and twenty-two of these buildings had reached a point where it was possible to determine the number of additional beds provided, which amounted to 51,207.

DISCOVERING THE OBVIOUS

The United States Department of Agriculture reports on part of "a nation-wide study of how much money the American family makes and how it is spent." This proves once more that low income families consult dentists less frequently than doctors and that visits to the oculist usually are omitted entirely. It demonstrates again that persons with an annual income of less than $500 spend less for medical care than higher income families. It was also discovered that "a majority of families with very low incomes did not have periodic physical examinations by a doctor." The report does not state whether those with higher incomes had such periodic physical examinations. What this report and all others like it fail to tell is that almost all that is being done about this condition is due to the action of organized medicine and individual physicians, assisted by relief appropriations in some cases. Neither, of course, are any comparisons made to indicate whether the medical care received by members of the same income levels in other countries is as good as or better than the care received in the United States.

INCOMES OF PHYSICIANS

A survey of the income of some types of professional workers by the United States Bureau of Foreign and Domestic Commerce is summarized in the *Monthly Labor Review* (**47**:1114 [Nov.] 1938).

As table 1 shows, the number of practitioners in the sample was too small to make the estimates given reliable as measures of the income of all physicians. Nevertheless, the agreement of the figures given with other investigations lends some measure of confidence regarding the accuracy of the results.

An effort is also made to determine the income by years of experience. Here again the number in some years is so small as to indicate a large "probable error," which should be kept in mind in any use that may be made of these statistics.

TABLE 1.—*Net Income of Independent Professional Practitioners, 1929-1936*

Profession	1929	1930	1931	1932	1933	1934	1935	1936
Average Net Income								
Medical								
All practitioners	$5,298	$4,687	$4,065	$3,148	$2,909	$3,310	$3,629	$4,143
General practitioners	4,701	4,084	3,603	2,790	2,615	2,964	3,231	3,673
Specialists	8,314	7,734	6,402	4,964	4,397	5,112	5,636	6,521
Legal	†6,601	*	*	4,088	3,786	3,692	3,885	4,320
	‡5,561	*	*	*	3,273	*	*	3,725
Accounting								
C. P. A.	5,749	*	*	*	*	4,012	4,291	4,626
Non-C. P. A.	3,303	*	*	*	*	2,226	2,463	2,910
Dentistry	*	*	*	2,778	2,495	2,780	*	*
Percentages of 1929								
Medical								
All practitioners	100	88.5	76.7	59.4	54.9	62.5	68.5	78.2
General practitioners	100	86.9	76.6	59.3	55.6	62.8	68.7	78.1
Specialists	100	93.0	77.0	59.7	52.9	61.5	67.8	78.4
Legal	†100	*	*	61.9	57.4	55.9	58.9	65.4
	‡100	*	*	*	58.9	*	*	67.0
Accounting								
C. P. A.	100	*	*	*	*	69.8	74.6	80.5
Non-C. P. A.	100	*	*	*	*	67.4	74.6	88.1
Dentistry	*	*	*	*	*	*	*	*
Number of Practitioners in Sample								
Medical								
All practitioners	753	752	791	850	912	1,053	1,048	1,057
General practitioners	593	592	622	669	724	835	828	834
Specialists	160	160	169	181	188	218	220	223
Legal	†557	*	*	§685.8	734	777	787	§784.5
	‡706	*	*	*	944	*	*	1,157
Accounting								
C. P. A.	695	*	*	*	*	896	916	961
Non-C. P. A.	45	*	*	*	*	57	57	61
Dentistry	*	*	*	1,007	1,007	1,007	*	*

* Information not obtained for these years.
† Averages based on the questions asked by the Department of Commerce.
‡ Averages obtained from supplementary questions included for the American Bar Association.
§ Fractions indicate part of year participation in legal firms.

TABLE 2.—*Net Income and Percentage Distribution of Medical and Legal Independent Practitioners, by Years of Experience, 1936*

Years of Experience	Medical			Legal		
	Persons in Sample		Average Net Income	Persons in Sample		Average Net Income
	Number	Per Cent		Number	Per Cent	
Total	1,378	100.0	.....	1,090	100.0	.....
1 year	16	1.1	$ 925	30	2.7	$1,059
2 years	49	3.6	1,839	53	4.9	1,121
3 years	79	5.7	2,747	48	4.4	1,630
4 years	50	3.6	3,060	59	5.4	1,779
5 years	45	3.3	3,558	60	5.5	2,047
6 years	45	3.3	3,622	54	4.9	2,176
7 years	30	2.2	3,693	42	3.9	2,375
1 to 2 years	65	4.7	1,614	83	7.6	1,090
3 to 7 years	249	18.1	3,229	263	24.1	1,990
8 to 17 years	302	21.9	4,930	326	29.9	3,629
18 to 27 years	278	20.2	4,983	207	19.0	4,893
28 to 37 years	323	23.4	3,717	139	12.7	4,964
38 to 47 years	142	10.3	2,525	53	4.9	4,016
48 to 52 years	17	1.2	1,600	13	1.2	2,591
Over 52 years	2	0.2	678	6	0.6	1,248

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ARIZONA

Annual Registration Due January 1.—Every person practicing medicine, surgery or osteopathy in Arizona is required by law to pay annually on or before January 1, to the board of medical examiners, a renewal license fee of $3. Any licentiate who does not renew his license as required is to be penalized $1 for each day that he practices without a renewal license, not to exceed $50. The board of medical examiners is to revoke the license of any licentiate who fails to renew his license for three successive years.

ARKANSAS

Annual Reregistration Due January 1.—Every licentiate of the Arkansas Eclectic Medical Examining Board must register annually with the secretary of the board between January 1 and the last day in February and pay a fee, if a resident of Arkansas, of $2, and, if a nonresident, of $4. The failure of a licentiate to pay the required fee by March 1 automatically suspends his right to practice while delinquent. If he fails for three successive years to pay the required fee his license is to be canceled, and thereafter he will be reinstated only on such a showing to the board of moral character and professional qualifications as would entitle the applicant to the issuance of an original license and the payment of the same fee as is required for the issuance of an original license.

CALIFORNIA

Annual Registration Due January 1.—Every practitioner of medicine and surgery holding a license to practice in California is required by law to register annually, on or before January 1, with the secretary-treasurer of the board of medical examiners and at that time to pay a fee of $2. Failure to pay the required fee within sixty days after January 1 works a revocation of a license and thereafter a license may be reissued only after application and the payment of a $10 penalty.

Four Persons Indicted for Treating Alcoholism.—Four persons were indicted by the grand jury November 19 on charges by the state board of medical examiners that a South American arrow poison had been used in the treatment of alcoholic addicts, according to the newspapers. Under indictment were Thomas F. H. Huston, proprietor of the "Samaritan Treatment," an establishment offering to cure alcoholism, and his assistant, John A. Stevens, neither of whom has a medical degree; and two nurses, Ruth Nielsen and Juanita Butcher. It was stated that more than 200 complaints have been received by the state board against the treatment. The newspapers reported that two investigators for the board found that curare was used in the treatment.

Positions Open for Physicians.—The state personnel board announces several positions open for physicians, the examinations to be held January 5. There are vacancies for physician and internist, junior physician, physician (eye, ear, nose and throat) and physician and surgeon. Applications by nonresidents must be filed by December 26. Examinations will be held in San Francisco, Los Angeles, San Diego, Sacramento, Fresno, New York, Chicago, St. Paul, Madison, Wis., Washington, D. C., Denver, Portland, Ore., Seattle, Dallas, Texas, Columbus, Lansing, Mich., Jacksonville, Fla., Baltimore, Boston, and Phoenix, Ariz., and such other cities outside the state of California as the number and location of candidates may warrant. Information may be obtained from the state personnel board, 1025 P Street, Sacramento.

CONNECTICUT

Personal.—Dr. Julius Lane Wilson, assistant clinical professor of medicine, Yale University School of Medicine, New Haven, has been appointed associate professor of medicine at Tulane University of Louisiana School of Medicine, New Orleans.——Dr. Russell V. Fuldner, chief, division of crippled children, state department of health, Hartford, has resigned to accept a residency in orthopedic surgery at Massachusetts General Hospital, Boston.

Annual Registration Due During January.—Every practitioner of medicine and surgery holding a license to practice in Connecticut is required by law to register during January with the state department of health and at that time to pay a fee of $2. Licentiates who have retired from active practice or who live out of the state must register annually but need not pay a fee. A practitioner failing to register is liable to a fine of not more than $5.

Exhibition of Rare Medical Volumes.—Yale University School of Medicine, New Haven, recently sponsored an exhibition of books commemorating the two hundredth anniversary of the death of Hermann Boerhaave, professor of botany, chemistry and clinical medicine at the University of Leyden. Boerhaave was born in 1668 and died in 1738. Lent by Dr. John F. Fulton, Sterling professor of physiology at Yale, the books included a first edition of Boerhaave's "Institutiones Medicae," published in 1708, which for the first time established physiology as an academic discipline in the medical curriculum, according to *Science*, and was written to give his students a background of knowledge of normal function; in the work he introduces the term "physiology" in its modern connotation.

FLORIDA

Annual Registration Due January 1.—Every practitioner of medicine and surgery holding a license to practice in Florida is required by law to register annually on or before January 1 with the secretary of the state board of health and at that time to pay a fee of $1. A licentiate failing to register annually is liable to a fine of not more than $50.

Personal.—Dr. Terry Bird, Tavares, has been appointed in charge of the newly created Lake County health unit.—Dr. James Maxey Dell Sr., superintendent of the Florida Farm Colony, was named mayor-commissioner of Gainesville recently, succeeding R. B. Livingston.——Dr. Lauren M. Sompayrac, Jacksonville, was recently awarded the Robert L. Schermer Cup by the local junior chamber of commerce in recognition of his "meritorious leadership" during the past six months. Dr. Sompayrac graduated from the University of Pennsylvania School of Medicine, Philadelphia, in 1935.

ILLINOIS

Society News.—Dr. Norbert C. Barwasser, Moline, discussed the management of common skin diseases before the Whiteside County Medical Society, Sterling, November 21.—The Peoria City Medical Society was addressed November 1 by Lewis Gerber, Ph.D., on "Recent Advances in Clinical Chemistry" and Dr. Hugh E. Cooper on "Fractures of the Shaft of the Femur."——Dr. Edmund F. Foley, Chicago, discussed "Jaundice: Its Clinical Significance" before the Adams County Medical Society in Quincy November 14.——Dr. Fred W. Bailey, St. Louis, discussed "Nonpenetrating Intra-Abdominal Injuries" before the Madison County Medical Society in Alton November 4.

Chicago

Lectures on Psychoanalysis.—A group of introductory lectures on psychoanalysis began at the University of Illinois College of Medicine November 30 under the auspices of the Institute for Psychoanalysis. Dr. Franz Alexander, director of the institute, is making a systematic presentation of medical psychoanalysis. Sixteen weekly lectures make up the course, which carries a fee of $10.

Society News.—The Chicago Laryngological and Otological Society was addressed November 7 by Drs. Ellison L. Ross on "Experiences with a Vital Stain in Otolaryngeal Tissues"; Frank E. Simpson, "Intrinsic Carcinoma of the Larynx—A New Instrument Modeled After the Jackson Bronchoscope for the Intralaryngeal Application of Radon," and Hans Brunner, "Inflammatory Diseases of Meninges and Brain of Pharyngeal Origin."——Dr. Frederick A. Coller, Ann Arbor, Mich., discussed "Hypochloremia Associated with Surgical Diseases" before the Chicago Surgical Society November 4; Drs. Loyal Davis and John Martin, "Surgical Aspects of Paratrigeminal Lesions," and Geza DeTakats, "Observations of Congenital Megacolon."

KENTUCKY

Date of Dr. J. N. McCormack's Death.—In the news item concerning the new building of the Kentucky State Board of Health and the Kentucky State Medical Association recently dedicated as a memorial to Dr. Joseph N. McCormack, published in THE JOURNAL December 10, page 2219, the date of Dr. McCormack's death should have been May 4, 1922, instead of Aug. 4, 1922.

LOUISIANA

Annual Renewal Due January 1.—Every practitioner of medicine and surgery holding a certificate to practice in Louisiana is required by law to have his certificate renewed annually on or before January 1 by the secretary-treasurer of the state board of medical examiners and at that time to pay a fee of $2. The board may by unanimous vote revoke any certificate not renewed.

Society News.—At a meeting of the Orleans Parish Medical Society in New Orleans November 14 Drs. Richard S. Crichlow spoke on "Treatment of Headache with Theelin"; Upton W. Giles, "The Historical Development and Modern Application of Artificial Fever," and George Gordon McHardy III, "Peritoneoscopy." —— Dr. Edward Garland Walls was recently elected president of the New Orleans Eye, Ear, Nose and Throat Club and Dr. William B. Clark secretary-treasurer.

MASSACHUSETTS

Infectious Encephalitis Made a Reportable Disease.—At a meeting of the public health council in Boston October 11 it was voted to substitute the term "infectious encephalitis" for "encephalitis lethargica" on the list of reportable diseases in Massachusetts. The change was made because of the belief that the term "encephalitis lethargica" is not broad enough to include all cases of encephalitis that are of possible danger to public health. The new terminology will exclude encephalitis caused by chemicals and degenerative changes. On the other hand, "infectious encephalitis" should include cases of encephalitis which appear to result from an apparent communicable disease or vaccination.

Dr. Christian to Retire from Brigham Hospital.—Dr. Henry A. Christian, Hersey professor of the theory and practice of physic, Harvard Medical School, Boston, will retire next September as physician-in-chief of Peter Bent Brigham Hospital, a position he has held since the hospital was completed in 1912. A portrait of Dr. Christian was presented to the hospital corporation October 13 at a gathering of 350 friends and pupils. Dr. Christian received his medical degree at Johns Hopkins University School of Medicine, Baltimore, in 1900. He was pathologist at the Boston City Hospital from 1900 to 1905 and at the Children's Hospital, Boston, 1903 to 1905. During the latter period he taught pathology at the Harvard Medical School, changing in 1905 to the theory and practice of physic, becoming Hersey professor in this subject in 1908. He was dean of the medical school from 1908 to 1912 and physician-in-chief to Carney Hospital from 1907 to 1912. He was secretary of the Section on Pathology and Physiology of the American Medical Association from 1903 to 1905, chairman of the section from 1905 to 1907 and of the Section on Practice of Medicine, 1916-1917. He was resident chairman of the division of medical sciences of the National Research Council, 1919-1920; president of the American Society for Clinical Investigation in 1919 and the Association of American Physicians in 1935. He is editor for the Oxford University Press of Oxford Medicine and Oxford Monographs and has contributed extensively to medical literature. On his sixtieth birthday in 1936, Dr. Christian was presented with a volume of medical papers dedicated to him by his former students and colleagues.

MINNESOTA

Annual Registration Due During January.—Every practitioner of medicine and surgery holding a license to practice in Minnesota is required by law to register annually during January with the secretary of the board of medical examiners and at that time to pay a fee of $2. A licentiate who practices without renewing his license is guilty of a misdemeanor and is liable to prosecution.

MISSOURI

Pilgrimage to Beaumont's Grave.—The St. Louis Medical Society conducted its annual birthday pilgrimage to the grave of William Beaumont November 21. Rev. Harry B. Crimmins, S.J., president of St. Louis University, where Beaumont was the first professor of surgery, was the speaker.

Society News.—At a meeting of the Boone County Medical Society in Columbia October 4 the speakers included Dr. William J. Stewart, Columbia, on "The Smith-Petersen Nail in Treatment of Fractures of the Femur."——At a meeting of the Buchanan County Medical Society in St. Joseph November 2 Dr. Thomas L. Howden discussed "Common Types of Neuroses." —— The Southeast Missouri Medical Society held its sixty-second annual meeting at Poplar Bluff October 11-12. Dr. George W. Vinyard, Jackson, the only living charter member of the society, was present. Dr. Bernard J. Macauley, Poplar Bluff, was chosen president and Cape Girardeau was selected as the place of the next annual meeting in October.

NEW JERSEY

Scarlet Fever Isolation Period Reduced.—The state department of health recently amended the state sanitary code to reduce the minimum period of isolation of cases of scarlet fever. The amendment, which went into effect October 1, changes the quarantine from thirty to twenty-one days.

Second Councilor District Meeting.—At a meeting of the Second Councilor District of the Medical Society of New Jersey in Jersey City December 15 the speakers were Drs. Morris Fishbein, Chicago, Editor of THE JOURNAL, on "American Medicine and the National Health Program"; William J. Carrington, Atlantic City, president of the state society, "Medicine in the News," and Hilton S. Read, Atlantic City, "Voluntary Medical Costs Insurance."

Annual Health Meeting.—The sixty-fourth annual meeting of the New Jersey Health and Sanitary Association was held at Asbury Park November 18-19. There were sessions on cancer, mental hygiene and social hygiene, motion picture showings, a microscopic exhibit of common parasites in New Jersey and an exhibit of publicity material. Among the speakers were Drs. William G. Herrman, Asbury Park, chairman of the cancer control committee of the Medical Society of New Jersey, on "The Cancer Situation in New Jersey"; Clarence C. Little, Sc.D., Bar Harbor, Maine, managing director, American Society for the Control of Cancer, "The Public and Cancer Control"; Haven Emerson, New York, "Signs of the Times in Public Health," and Mr. Homer Calver, director of health exhibits, New York World's Fair, "Health Exhibits, World's Fair and Otherwise."

NEW YORK

Annual Graduate Lectures.—The eleventh annual series of graduate lectures sponsored by the Medical Society of the State of New York in Rochester was presented during October. The following addresses were given:

Dr. Samuel J. Kopetzky, New York, October 3, Recent Developments in the Treatment of Paranasal Sinusitis and Mastoiditis, Including the Use of Roentgenology and Chemotherapy.
Dr. Foster Kennedy, New York, The Organic Background of Mind.
Dr. Samuel W. Clausen, Rochester, Latest Developments in Vitamins.
Dr. Henry H. Ritter, New York, Treatment of Burns and Hand Infections.
Dr. Henry Rawle Geyelin, New York, Diabetic Coma.

Annual Registration Due January 1.—Every practitioner of medicine and surgery in New York is required by law to apply annually, on or before January 1, to the secretary of the board of medical examiners for a certificate of registration, on application forms furnished by him, and to pay at that time a fee of $2. The law authorizes the secretary of the board to permit secretaries of duly incorporated medical societies to act as his representatives, to receive and transmit to him such applications and fees. Practitioners are liable to severe penalties for failing to register and for continuing in practice thereafter.

New York City

Another Orchestra.—The Doctors' Musical Society of Brooklyn was recently organized and an orchestra is in process of formation. Dr. Harry Tevel Zankel, 614 Eastern Parkway, Brooklyn, is secretary.

Brickner Lecture.—The eighth Walter M. Brickner Lecture was given at the Hospital for Joint Diseases November 17 by Dr. Charles A. Elsberg. His subject was the orthopedic and neurologic significance of back pain.

Bronx Society to Honor Dr. Van Etten.—The Bronx County Medical Society will celebrate its twenty-fifth anniversary Jan. 7, 1939, with a dinner dance at which Dr. Nathan B. Van Etten will be the guest of honor. Dr. Van Etten, for several years medical director of Morrisania Hospital, was the first president of the Bronx County society. For three years Dr. Van Etten was Speaker of the House of Delegates of the American Medical Association, having retired at the San Francisco session in June. In 1925 he was president of the Medical Society of the State of New York.

Society News.—Drs. John G. Kidd and Fred W. Stewart, New York, addressed the New York Pathological Society November 18 on "Immunologic Studies with Virus-Induced and Transplantable Growths of Rabbits" and "Use

of the Aspiration Biopsy in Diagnosis of Tumors" respectively. Dr. Richard E. Shope of the Rockefeller Institute for Medical Research, Princeton, N. J., delivered the Middleton Goldsmith Lecture December 7 on "Complex Infections."——At a meeting of the New York Diabetic Association with the section of medicine of the New York Academy of Medicine December 20 the speakers will be Drs. Herman Lande, on "Present Status of Protamine Zinc Insulin Therapy"; Edward Tolstoi, "Protamine Zinc Insulin: A Metabolic Study of Two Severe Cases of Diabetes with Comments on Criteria for Treatment," and Henry Rawle Geyelin, "Management of Diabetic Acidosis and Its Accompanying Medical Shock."——Dr. William Osler Abbott, Philadelphia, will address the New York Roentgen Society December 19 on "The Role of Small Intestinal Intubation in the Treatment and Diagnosis of Intestinal Obstruction."

NORTH DAKOTA

Annual Registration Due January 1.—Every practitioner of medicine and surgery holding a license to practice in North Dakota is required by law to register annually on or before January 1, with the secretary-treasurer of the board of medical examiners and at that time to pay a fee of $5 if a resident of North Dakota or $2 if a nonresident. A practitioner may not lawfully practice if he has not registered. If he does so his license may be revoked and can be reinstated on the payment of unpaid fees and $0.50 for each month of default.

OHIO

Western Reserve Selected for Cancer Training Center.—The National Cancer Institute has chosen Western Reserve University School of Medicine as one of the centers for training of physicians in the diagnosis and treatment of cancer. Appointments are filled at present, but, as vacancies may arise, those interested should apply promptly to the Surgeon General, U. S. Public Health Service, Washington, D. C. Appointments are for two years, with eight months each of pathology, radiology and surgery. Applicants must have had at least three years of hospital training, one of which may have been a rotating internship; at least two years must have been in surgical experience. Not more than one trainee can be accepted at present, but the number may later be increased to three, according to the announcement. Trainees will be paid by the National Cancer Institute on a per diem basis, out of which they will be expected to pay all the necessary expenses, including tuition, if any is charged by the institution which accepts them for training. Stipends for training will range from a per diem allowance of from $5 to $10, depending on training, experience and other considerations. Further information and application blanks may be obtained on written request to the Surgeon General at Washington or from Dr. John H. Lazzari, Secretary of the Cancer Training at Western Reserve University, Republic Building, Cleveland, Ohio.

OREGON

Society News.—Dr. Herbert Van H. Thatcher, Portland, addressed the Central Willamette Medical Society, Newport, recently on "Injuries of the Hand."——Dr. Warren G. Bishop addressed the Jackson County Medical Society, Medford, recently on common colds.——Dr. Arthur J. McLean addressed the Multnomah County Medical Society, Portland, October 19 on "The Adequate Neurological Examination," and Dr. Homer P. Rush gave a demonstration of electrocardiography. The speaker October 5 was Dr. Robert W. Langley, Los Angeles, on "Heart Sounds: A Clinical Experiment in Sound Photography." The society held its first hobby show September 24 with sixty physicians as exhibitors; more than 1,000 persons attended.

PENNSYLVANIA

Annual Registration Due January 1.—Every practitioner of medicine and surgery holding a license to practice in Pennsylvania is required by law to register annually on or before January 1 with the board of medical education and licensure in the department of public instruction and to pay a fee of $1 or such fee as may be fixed by the department of public instruction. A practitioner who fails to register and who continues to practice is liable to a fine of from $10 to $100.

Society News.—Dr. Albert D. Ruedemann, Cleveland, addressed the Cambria County Medical Society, Johnstown, November 10, on "A Clinical Survey of 100 Cases of Headache."——Drs. Arthur Carlton Ernstene and Robert S. Dinsmore, Cleveland, addressed the Lycoming County Medical Society, Williamsport, at its annual clinic meeting November 11 on "Use of Drugs in Heart Disease" and "Problems in Thyroid Surgery" respectively.——Drs. Thomas B. Herron, Monessen, and Albert S. Sickman, Lock No. Four, addressed the Washington County Medical Society at Lock No. Four November 9 on "The Ruptured Appendix" and "Immediate Operation of Compound Fractures" respectively.——Dr. Edward S. Dillon, Philadelphia, addressed the Delaware County Medical Society, Chester, November 10 on "Diabetic Coma."——Dr. Charles F. Geschickter, Baltimore, addressed the Northampton County Medical Society November 17 on "Neoplasms of the Mammary Gland."

RHODE ISLAND

Subject for Fiske Fund Essay.—The trustees of the Fiske Fund, administered by the Rhode Island Medical Society, have chosen the following subject for the prize essay of 1939: "Cesarean Section—Indications and Contraindications for the Various Types of Operations." Competitors must forward to the secretary, Dr. Wilfred Pickles, 184 Waterman Street, Providence, copies of their dissertations before May 1, 1939. Each must be identified by a motto and accompanied by an envelop bearing the same motta on the outside and the name and address of the sender within.

SOUTH CAROLINA

Dr. Jervey Honored.—The Greenville County Medical Society held a dinner in honor of Dr. James W. Jervey, Greenville, then president of the Southern Medical Association, November 7 in Greenville. The speakers were Drs. William Weston, Columbia; Robert Wilson, Charleston; Frank H. McLeod and William S. Fewell, Greenville. At the society's meeting Drs. Edwin A. Merritt, Washington, D. C., and Kenneth M. Lynch, Charleston, spoke on "Carcinoma of the Cervix" and "The Evolution of Cancer Control and Knowledge" respectively.

Society News.—Dr. Addison G. Brenizer, Charlotte, N. C., addressed the Newberry County Medical Society, Newberry, November 10, on "The Evolution of Thyroidectomy." Other speakers were Drs. Austin T. Moore, on "Fractures—Some Fundamental Principles in Their Treatment"; Roger G. Doughty, "Head Injuries," and Lucius Emmett Madden, "Coronary Thrombosis"; all are of Columbia.——Dr. Rock Sleyster, Wauwatosa, Wis., President-Elect of the American Medical Association, addressed the Columbia Medical Society November 14 on "Medical Problems of the Day." Dr. George Bolling Lee, New York, addressed the society October 10, on "Chorio-Epithelioma" and Dr. James Heyward Gibbes, Columbia, on "Tick Paralysis as Indicative of Growing Menace from Ticks as Carriers of Disease."

TEXAS

Annual Registration Due January 1.—Every practitioner of medicine and surgery holding a license to practice in Texas is required by law to register annually on or before January 1 with the state board of medical examiners and at that time to pay a fee of $2. If a practitioner fails to renew his registration within sixty days after January 1 his license is suspended.

WEST VIRGINIA

Personal.—Dr. Norman G. Angstadt, New Martinsville, has been appointed health officer of Wetzel County to succeed Dr. John B. Hozier, acting health officer during the past year.——Dr. William A. Bevacqua, Charleston, has been appointed health officer of Parkersburg and Wood County to succeed Dr. Arthur D. Knott, Parkersburg, resigned.——Dr. David B. Ealy, Moundsville, was elected to the state senate in the November election.

Society News.—Dr. Edward M. Livingston, New York, addressed the Kanawha Medical Society, Charleston, October 11, on "Abdominal Pain."——Dr. Wilbur E. Hoffman, Charleston, addressed the Monongalia County Medical Society, Morgantown, October 4, on "Ruptured Uterus."——Dr. Vernon L. Peterson, Charleston, was the speaker at a meeting of the Raleigh County Medical Society, Beckley, October 20, on silicosis.——The Wood and Kanawha county medical societies held a joint meeting October 20 at the Spencer State Hospital. Drs. Jacob J. Alpers and Mark Thumin of the hospital staff read papers on shock therapy of mental patients. Dr. George D. Johnson, superintendent of the hospital, entertained the visiting physicians and the state board of control at a dinner in the hospital dining room.

GENERAL

Outbreaks of Tularemia.—Twelve deaths from tularemia have been reported in Illinois since the hunting season opened November 10, according to the newspapers of December 12. More than 250 cases have been reported. The sale and transportation of rabbits have been barred in East St. Louis, where twenty-six cases were reported within fifteen days. In Indiana fifty-five cases were reported in the first ten days of December, as compared with thirty-three cases during the entire month in 1937. Cases have been reported in Iowa and Ohio, although Illinois is said to be leading in prevalence.

Symposium on Glycols.—The pharmacy section of the American Association for the Advancement of Science will present a special session on glycols December 27 at the meeting in Richmond, Va. The speakers will be:

Frank C. Whitmore, Ph.D., State College, Pa., Chemistry of the Glycols.
Herbert O. Calvery, Ph.D., chief pharmacologist, Food and Drug Administration, U. S. Department of Agriculture, Washington, D. C., Pharmacology of the Glycols.
Mr. H. B. McClure, Carbide and Carbon Chemicals Corporation, Industrial Application of the Glycols.
Andrew G. DuMez, Ph.D., Baltimore, Pharmaceutical Uses of the Glycols.

Discussion will be opened by Drs. Harvey B. Haag, Richmond, and Michael G. Mulinos, New York.

Society News.—The National Gastroenterological Association announces that it has taken an office with its official publication, the *Review of Gastroenterology*, at 1819 Broadway, New York.——The sixteenth annual meeting of the American Orthopsychiatric Association will be held in New York at the Hotel Commodore, Feb. 23-25, 1939. Dr. Norvelle C. LaMar, New York, is the secretary.——The Pacific Coast Surgical Association will hold its next annual session in San Francisco, Oakland and Del Monte, March 28-31, 1939. Dr. Harry Glenn Bell, University of California Hospital, San Francisco, is the secretary.——Dr. Jennings C. Litzenberg, Minneapolis, was chosen president-elect of the Central Association of Obstetricians and Gynecologists at its annual meeting in Minneapolis in October. Dr. Ralph A. Reis, Chicago, became president and Dr. Thomas B. Sellers, New Orleans, was elected vice president. Dr. William F. Mengert, Iowa City, was reelected secretary.

Posthumous Award of Sedgwick Medal.—The American Public Health Association at its meeting in Kansas City October 25-29 awarded its Sedgwick Medal posthumously to Dr. Wade Hampton Frost, professor of epidemiology at Johns Hopkins University School of Hygiene and Public Health, Baltimore, who died May 1. Dr. Frost served as dean of the Johns Hopkins school of hygiene from 1931 to 1934 and had been professor since 1921. He was associated with the U. S. Public Health Service from 1905 to 1929. During the World War he was director of the bureau of sanitary science of the American Red Cross. In a statement at the meeting in Kansas City Dr. Haven Emerson, New York, on behalf of the medal committee, said: "While his illuminating contributions in the fields of poliomyelitis, influenza, diphtheria and tuberculosis stand high among the classics of epidemiology, perhaps his planning, direction and guidance of the stream pollution laboratory at Cincinnati will prove to have been his most abundant legacy to the expanding fields of the theory and practice of public health."

Southwestern Medical Association.—The annual session of the Southwestern Medical Association was held in El Paso October 28-29 with headquarters at the Hotel Cortez. The guest speakers were:

Dr. Charles A. Bahn, New Orleans, Prevention of Blindness from the Standpoint of the General Practitioner; Practical Ophthalmic Advances for the General Physician.
Dr. Horton R. Casparis, Nashville, Public Health Aspects of Childhood Tuberculosis; Medical Aspects of Healthy Child Behavior; Allergy in Children.
Dr. George T. Caldwell, Dallas, Texas, Estimation of Kidney Function; Pathology of Vitamin Deficiencies.
Dr. Raymond W. McNealy, Chicago, Preoperative Management of the Jaundiced Patient; Dietary Deficiencies in Surgical Patients; Management of Blood Vessel Injuries and Their Sequelae.
Dr. Edward H. Rynearson, Rochester, Minn., Complications of Diabetes; Present Day Methods of Treating Goiter; Recent Advances in Endocrinology.
Dr. Curtice Rosser, Dallas, Texas, Diagnostic Criteria of Rectal Cancer; Rational Management of Hemorrhoids; Rational Management of Minor Anal Conditions.
Chauncey D. Leake, Ph.D., San Francisco, Antiseptic Agents; Epinephrine, Ephedrine and Their Derivatives; Art in Medicine.

Dr. Orville E. Egbert, El Paso, was chosen president-elect of the association and Dr. Howell S. Randolph, Phoenix, Ariz., was installed as president. Drs. Ralph W. Mendelson, Albuquerque, N. M., and Jesse D. Hamer, Phoenix, were elected vice presidents and Dr. Maurice P. S. Spearman, El Paso, Texas, is secretary.

Foundation for Infantile Paralysis Extends Organization.—A new plan of organization in county units was adopted by the National Foundation for Infantile Paralysis at a meeting of its trustees and officers in New York November 10. Permanent county chapters are to be organized as fast as possible after the campaign for funds, which will reach its climax on President Roosevelt's birthday, Jan. 30, 1939. In addition to the plan for field organization, the officials of the foundation decided that the funds raised this year will be divided on a 50-50 basis, half to be sent to the national committee and half to be retained in the counties where the money is raised. It is planned that county chapters will work closely with the national committee in helping victims of poliomyelitis, in disseminating knowledge of diagnosis and treatment and in emergencies in times of epidemics. Funds left in the counties will be held as trust funds for the account of the national foundation and will be administered under general rules and regulations laid down by the national foundation, according to the announcement, but within those limitations expenditures will be in the discretion of the local chapter or unit.

Low Tuberculosis Mortality Rate.—The National Tuberculosis Association, which opened its thirty-second annual sale of Christmas seals Thanksgiving Day, announces that the death rate from tuberculosis dropped from 55.5 per hundred thousand in 1936 to 53.5 in 1937, the lowest ever reported. The 1936 rate was the highest in ten years, an increase attributed to the cumulative effects of the depression. In 1936 71,239 persons died of tuberculosis and in 1937 the number was 69,151. Fifteen states showed an increase over 1936, but this was more than balanced by decreases in thirty-two states. Michigan's rate remained the same and the District of Columbia showed a decrease. Among the states in which notable decreases were reported were: Arizona, 258.5 from 271.2 the previous year; Maine, 33.5 from 40.6; New Hampshire, 28 from 33.9; North Carolina, 54.8 from 60.8; Tennessee, 84.7 from 89.6, and Virginia, 59.4 from 64.2. Wyoming reported a rate of 18.3, the lowest of any state, though it was an increase from 15 reported in 1936. The highest rates were in Arizona and New Mexico, with 258.5 and 113.3 respectively, followed by the District of Columbia with 94.9. Case finding activities increased in twenty-seven states, according to the report. Thirteen states and the District of Columbia exceeded the standard ratio of two new cases reported to each death in any year. The states were Connecticut, Idaho, Illinois, Maryland, Massachusetts, Michigan, Minnesota, Montana, New Jersey, New Mexico, New York, Oregon and Washington.

Government Services

Dr. McIntire Appointed Surgeon General of Navy

President Roosevelt announced November 29 the appointment of Dr. Ross T. McIntire, who for five years has been White House physician, as surgeon general of the U. S. Navy, with the rank of rear admiral. Dr. McIntire was first commissioned in the navy in 1917 and his rank was that of commander, although he was temporarily a captain at the time of his latest appointment. The President has not yet announced the appointment of the new White House physicians, of whom there will be two from now on, according to newspaper reports. Dr. McIntire was born in Salem, Ore., Aug. 11, 1888, graduated from the Willamette University Medical Department, Salem, in 1912 and was first commissioned in the medical corps of the navy April 4, 1917. Prior to assignment to duty as White House physician he was in charge of the eye, ear, nose and throat service at the Naval Hospital in Washington. As Surgeon General he succeeds Dr. Perceval S. Rossiter, who retires from active service because of the age limit. In reaching the rank of rear admiral, Dr. McIntire, in service parlance, was jumped over the heads of thirty-four commanders and eighty-four captains. A native of Shepherdstown, W. Va., Dr. Rossiter has been a member of the medical corps of the U. S. Navy since 1903. He was a member of the U. S. Naval Mission to Brazil, 1922-1926; commanding officer of the Brooklyn Naval Hospital, 1929-1932, Washington, D. C., Naval Hospital, 1932-1933. In 1933 he became surgeon general. He graduated at the University of Maryland School of Medicine, Baltimore, in 1895.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Nov. 19, 1938.

The Public Health

The report for 1937 of the chief medical officer of the Ministry of Health, which has just been published, shows that the birth rate was 14.9 per thousand living, a slight rise on 14.8 for 1936 and 0.5 above that for 1933, which was the lowest on record. The infant mortality was 58 per thousand births, against 59 for 1936, but one point higher than the exceptionally low figure of 57 in 1935. The five principal killing diseases remain the same as for many years and in the same order: (1) diseases of the heart and circulatory system, (2) malignant disease, (3) respiratory diseases, (4) diseases of the nervous system, (5) tuberculosis. But if the diseases are arranged to show the principal killing diseases in the years of working life from 15 to 65 years, tuberculosis takes the third place and diseases of the nervous system the fifth. There has been a decline in the incidence of lethargic encephalitis and scarlet fever but an increase in that of cerebrospinal fever, diphtheria, dysentery, influenzal pneumonia and acute poliomyelitis. The maternal mortality continues to fall, being 3.13 against 3.65, 3.94 and 4.41 in 1936, 1935 and 1934. Puerperal sepsis accounted for 0.94 per thousand, leaving 2.19 for other causes. There is evidence that fresh infection with syphilis is declining. There is no evidence that cancer is becoming less prevalent. More than half as many males were killed by injury as by all the infectious diseases taken together, and a large proportion of these violent deaths occurred on the roads. Statistical inquiry has revealed that there are accident-prone just as there are sickness-prone persons, i. e., persons for whose abnormal sickness rate no physical grounds can be assigned and malingering can be excluded. A great extension has been made of the scheme of graduate education for panel physicians, who it is intended will receive a free course every five years. Not only will the course be paid for but also traveling and subsistence costs and the cost of a locum tenens when one is necessary.

Rectal Ulceration Due to Cancer of Cervix

When new drugs are found valuable in treatment it is only later and gradually that their possible toxic effects become evident. The same statement holds true for radiotherapy, which has proved such an important advance in the treatment of cancer. It is only recently that it has been discovered that the radium treatment of cancer of the cervix uteri may produce chronic ulceration of the rectum. But little has been published on the subject, and the pathology of the condition has not been described. During the tenure of a research scholarship at the Christie Hospital and Holt Radium Institute, Manchester, Mr. T. F. Todd has had personal experience in thirty-four cases of chronic ulceration of the rectum in 800 cases of cancer of the cervix treated by radium. In a report to the North of England Obstetrical and Gynaecological Society he stated that this reaction was frequently overlooked and several cases were referred after previous radium treatment elsewhere for what was misdiagnosed as cancer of the rectum. The cases were of two types: 1. A lesion restricted to the anterior rectal wall, usually at the level of the cervix uteri, forming a mobile ulcerated mass from 3 to 5 cm. in diameter and resembling an operable carcinoma. 2. A rectal ulceration similarly situated, but accompanied by gross perirectal induration and formation of a hard fixed mass enveloping the rectum and anchoring it to the sacrum, resembling advanced inoperable cancer with extensive extrarectal spread. In its early stage the rectal ulceration took the form of acute proctitis. The reaction might be due to overdosage from slipping of the radium applicators and their approximation to the rectum in the posterior fornix or to retroversion which allowed the intra-uterine applicator to project against the rectum. The main factor appeared to be obliteration of blood vessels from the high dosage.

The symptoms usually began after from six to nine months' treatment. They included tenesmus, melena and severe pain. Spontaneous healing was the rule, but stenosis of the rectum might occur and require colostomy. The incidence of the ulceration could be reduced by precautions to avoid misplacement of the vaginal applicators and overdosage and by nursing patients in the prone position. In four cases presacral neurectomy was done for the relief of pain and acceleration of healing. It was suggested that it might act as a prophylactic against massive perirectal fibrosis by producing vasodilatation.

Toxic Effects of Sedormid

Attention has recently been directed to the toxic effects of the hypnotic sold under the name of sedormid (allyl-isopropyl-acetyl-carbamide). A number of cases of purpura haemorrhagica have been recorded. In the *Lancet,* Miller and Rosenheim suggest that it is a dangerous drug. They report a case in which a woman physician aged 26 was given two tablets of sedormid nightly while convalescent after thyroidectomy. She found it an excellent hypnotic, but after six weeks' use a widespread purpuric rash appeared. Though the drug was stopped she became acutely ill and the purpura was complicated by severe epistaxis. Her blood films showed almost complete absence of platelets, and despite three transfusions the hemoglobin fell in ten days to less than 30 per cent. Two further transfusions were necessary before the platelet counts began to increase. Discussing two cases of severe thrombocytopenic purpura due to the use of sedormid for insomnia, in the *British Journal of Dermatology,* the editor (Dr. A. C. Roxburgh) states that he has seen two cases of eruption, not purpuric, due to this cause. Both patients were women between 60 and 70 years of age. In one there was a red circinate eruption on the neck, cheeks, upper part of the back, sternum and backs of the hands. In the other patient there was a red scaling patch measuring 1 by 1½ inches on the back of the forearm, raised about one-fourth inch. It took several weeks to disappear. In both patients the eruption ceased after the sedormid was stopped but it recurred in the first patient when she resumed the drug.

The British Heart Journal

With the beginning of the new year the British Medical Association will publish a quarterly journal devoted to disease of the heart and circulation under the title of the *British Heart Journal.* This journal, which is being published at the request of the Cardiac Society of Great Britain and Ireland, will be edited by the cardiologists Dr. Maurice Campbell and Dr. Evan Bedford. The *British Medical Journal* states that, as diseases of the heart and circulatory system are the first of the principal causes of death at all ages in this country, it is a matter of surprise that such a journal is not already in existence. This does not overlook *Heart,* which for many years was edited by Sir Thomas Lewis and held a unique position among the medical periodicals of the world—a position still maintained with change of title to *Clinical Science* but happily without any change of editor. The research in experimental medicine that is carried out by Sir Thomas Lewis and is reported in this journal is of supreme importance to medicine and represents a field that probably will be only incidentally surveyed in the *British Heart Journal.* The new periodical will deal with work more concerned with the everyday diagnosis and treatment of patients and so will be of immediate value to the practicing physician. The appeal will be to the cardiol-

ogists, both at home and in other countries, but the journal is commended to all physicians "to whom the stethoscope of Laënnec has become the badge of their tribe." In form it will be similar to the other two special journals published by the *British Medical Association*. The subscription will be $6 a year.

PARIS

(From Our Regular Correspondent)

Nov. 19, 1938.

Recovery from Meningococcic Meningitis After the Use of Sulfanilamide

At the October 14 meeting of the Société médicale des hôpitaux of Paris Dr. R. A. Marquezy and his associates reported two cases of meningitis due to the meningococcus in which recovery followed the administration of sulfanilamide alone. In all cases which have previously been reported, chemotherapy was preceded by serotherapy. The authors cited a study by Muraz, Chirle and Queguinier (*Presse médicale*, July 16, 1938) of 397 cases of meningococcic meningitis treated during an epidemic of the disease in French Nigeria. The mortality in forty-nine cases in which serum alone was given was 22.44 per cent; in twenty-three cases in which serum and sulfanilamide (by mouth) were given, 8.7 per cent; in thirty-nine cases in which sulfanilamide given by mouth was preceded by one intraspinal injection of the drug, 15.38 per cent; in ten cases in which sulfanilamide given by mouth was preceded by two intraspinal injections of the drug, no deaths, and in 271 cases in which sulfanilamide given by mouth was the only therapy, 10.7 per cent.

In both of the cases reported by Marquezy and his associates, only sulfanilamide was given. The first patient, a boy aged 16, was given 7 Gm. a day by mouth for the first seven days and gradually decreasing amounts during the next twelve days. In addition, an intraspinal injection of an 0.8 per cent solution was given daily for fifteen days, the average amount being 10 cc. The second patient, a man aged 25, was given sulfanilamide only by mouth. Intraspinal administration is preferable at the onset as it secures a concentrated solution of the drug in the spinal fluid at the earliest possible moment.

In the discussion Dr. Weill-Hallé reported an additional case with recovery, in which only sulfanilamide was employed. Dr. Marquezy stated that sulfanilamide had not been found to be of any value in a personally observed case of pneumococcic meningitis. Dr. Benda suggested the use of sulfanilamide-pyridine in such cases.

French Otorhinolaryngologic Congress

The president of this year's meeting of the French Otorhinolaryngologic Congress, held in Paris October 24-26, was Dr. le Mée. The subject of the first report, by Drs. Collet and Mayoux of Lyons, was auricular tuberculosis. Although it is generally taught that from 5 to 10 per cent of the cases of chronic otitis media and mastoiditis are of tuberculous origin, the authors believe that this percentage is far too low, because in many cases the disease is not correctly diagnosed. Tuberculous otitis is at times observed clinically as an associated condition with pulmonary tuberculosis. Usually, however, the condition occurs independent of pulmonary localization. The clinical picture then differs considerably from that observed when it is an associated condition. Most commonly there is a history of an acute onset, resembling in every respect the clinical picture in cases of ordinary nontuberculous otitis. With children, tuberculous otitis should be thought of if there has been exposure to tuberculous adults, if the granulation tissue formed after a mastoid operation is flabby and pale and contains caseous particles, and if a fistula persists after mastoidectomy. In all such cases a search for underlying tuberculosis must be made with the aid of the guinea pig inoculation method. This had confirmed the clinical diagnosis in twenty-two cases. The prognosis, unless pulmonary lesions exist, is far more favorable than is generally believed. The treatment is surgical followed by heliotherapy and actinotherapy. As to the pathogenesis, the authors were of the opinion that the infection was primary in the nasopharynx and involved the middle ear by way of the eustachian tube.

TUMORS OF HYPOPHARYNX AND LARYNX

The subject of the second report, by Drs. Huët of Paris and Péri of Algiers, was roentgenologic exploration of tumors of the hypopharynx and larynx. The first objective in exposing films is to obtain profile views of the hypopharynx and larynx. The second objective is to secure anteroposterior views. The various technical methods to secure satisfactory exposures were described in detail. At the Paris Cancer Institute it has been found that 60 per cent of tumors of the hypopharynx originate in the piriform sinuses. Some are very radiosensitive and show but little tendency to extension, whereas others are very malignant. The remainder of this thorough review of the roentgenologic methods of diagnosis contained chapters on the search for endolaryngeal tumors and lesions of the cartilages.

POLYPS OF LARYNX; MENINGITIS

Drs. Piquet and Boury of Lille reported four cases of malignant changes in polyps of the larynx; hence every papilloma should be regarded as a potential cancer. Dr. Leroux-Robert said that a polyp was a purely inflammatory lesion and must be distinguished from a papilloma. The latter was a precancerous condition, but this was not true of a polyp. This point of view was confirmed by Professor Lemaitre of Paris.

Dr. Marcel Ombredanne of Paris reported three cases of streptococcic meningitis of otitic origin in which recovery had followed the use of a preparation similar to sulfanilamide. In only one of the three cases had the drug been employed exclusively, i. e., no operation performed. Those who took part in the discussion of this paper believed, however, that it is advisable always to operate and to give the drug as an adjuvant.

BERLIN

(From Our Regular Correspondent)

Nov. 8, 1938.

The Extent of Poliomyelitis in Germany

For several years a number of cases of epidemic poliomyelitis have been reported each summer from some part of the German reich. The locality affected varies from year to year. In general a year of severe epidemic is succeeded by several years during which the erstwhile stricken community remains more or less spared from the disease. An official survey just published by the national health bureau traces the incidence of the disease in Prussia since 1909 and in the entire reich since 1924. In 1909 a great wave of poliomyelitis occurred in Germany. Yet as soon thereafter as 1910 poliomyelitis had become a fairly rare disease. Not until 1926 did the morbidity rise again and in 1927 it attained a new peak with 2,840 cases. In 1928 the number of new cases again dropped to one third of the corresponding number for 1927. Thereafter the morbidity slowly increased from year to year until 1932. The latter year was marked by a severe epidemic (the most severe thus far, the cases numbering 3,869). In 1933 the number receded to one-third that of the previous year. Subsequently and down to date it has developed a gradual upward trend from one year to another. There were 2,256 cases reported in 1936 and 2,723 in 1937. According to these official statistics the 1938 figure will be higher than that for 1937.

In other countries also greatly increased incidences have been noted in recent years, particularly in the Scandinavian lands since 1934 and in Austria, Switzerland and Italy since 1936. At present an increased morbidity is reported from the Nether-

lands, whereas in the other foreign countries mentioned no especially notable increases have been reported during the current year.

A detailed survey shows that the region of highest morbidity within the reich changes from one year to the next in a desultory manner. An explanation of the erratic fluctuations in the waves of anterior poliomyelitis is to be found in the immunity against repetition of infection conferred by recovery. Thus only after a new generation of children has arisen will the contagion again encounter a large number of susceptible persons. However, the morbidity of poliomyelitis even in times of epidemic never suffices to immunize the entire population, since the disease is, after all, rare. This is shown by the following comparison: In 1937 there were 2,723 cases of poliomyelitis against 146,733 cases of diphtheria. Accordingly it must be that the majority of children either are not susceptible to infection by the agent of poliomyelitis or do not react to this infection in such a way as to produce the typical disorder with its concomitant paralysis. Even the so-called silent infections can confer immunity against later contagion. "Silent" infections are much more frequent than the forms that run a severer course.

With the end of the short-lived seasonal wave the local prevalence of the contagion tends to subside and soon disappears almost completely. The location and severity of the next year's epidemic cannot be foretold. A strong impetus has recently been given to investigation of the many as yet unsolved problems relative to ways and means of combating poliomyelitis. A new plan of therapy, based on uniform points of view, has been instituted in the hospitals of Berlin and of Hamburg. The experimental studies are concerned with the determination of the protective value of convalescent serum. Attempts have also been made to determine for how long and in what quantity protective substances are present in human beings following recovery from poliomyelitis as well as the protective value of the serum of healthy persons from the environment of patients with poliomyelitis. Finally, closer studies of the virus have been attempted by its cultivation. Only within the next few years will the results of this research be evaluated.

The Number of New Medicaments in Germany

The association of manufacturers of chemical-pharmaceutic preparations, an organization that represents thirty-seven leading German firms, reports that during 1935, 1936 and 1937 a total of 174 new specialties were placed on sale, whereas 108 specialties were withdrawn from the market. Accordingly the total number of these firms' pharmaceutic products on the market during the past three years increased by sixty-six. On April 1 these firms had 1,314 specialties on the market; if particular medicinal forms are considered, this total reaches 1,969.

Judging by the flood of pharmaceutic products in the German market, the quoted figures suggest that pharmaceutic houses both inside and outside the manufacturers' association bring out a vast number of so-called pharmaceutic agents (arzneimittel), which for the most part contain no new principle but rather—and this is still considered good form—merely represent the same or similar products under new names. In any event the regulation of the pharmaceutic industry, long urged by representatives of the medical profession, has not yet taken place, even with regard to the public declaration of every pharmaceutic product prescribed by a physician.

The Importance of Ewe's Milk in the Diet

Ewe's milk in the diet was the object of investigations undertaken by the Breslau University institute of animal husbandry and milk economy, the experimental research station for animal husbandry at Kraftborn and the Breslau Municipal Hospital for Nurslings and Infants. The principal investigators were W. Zorn, F. Richter and C. Wiener. With respect to the importance of ewe's milk in the national food economy it was estimated that there is an annual world yield of 5 billion liters, as against 17 billion liters of goat's milk and 270 billion liters of cow's milk. Europe produces 44 per cent of all ewe's milk and thus stands far ahead of Asia and Africa. Of all European countries Italy is the largest producer of ewe's milk, the yield there being 620 million liters yearly; Germany produces only 20 million liters of ewe's milk yearly (as against 24 billion liters of cow's milk).

To determine the suitability of ewe's milk as a food for nurslings, the investigators carried on feeding experiments, the results of which are reported in the journal *Ernährung*. The quality of ewe's milk with respect to its ingredients is greatly dependent on the state of lactation, even in comparison with cow's milk and human milk. Ewe's milk is far superior to human milk and cow's milk in fat, protein and mineral content and consequently in caloric content. Further questions studied were whether nurslings previously nursed by the mother ought to be put on ewe's milk, whether children who have been receiving cow's milk should be given ewe's milk instead and whether dyspepsia in nurslings can be dietetically treated with ewe's milk. It was found that artificial feeding of nurslings with ewe's milk is readily practicable and that it is even more easily accomplished and leads to better results than feeding with cow's milk. Even if the nurslings were suddenly taken off cow's milk and placed on ewe's milk, the substitution was always satisfactorily accomplished, and if the babies had been affected with acute gastro-enteric catarrh when fed with cow's milk quick remission of this dyspepsia took place when they were fed with ewe's milk.

Appointment to Chair of Psychiatry at Berlin

A short time ago Prof. Karl Bonhoeffer, since 1912 ordinarius in psychiatry at Berlin and now 70 years old, was retired from his post. Bonhoeffer had an excellent record as director of the clinic for psychiatric and nervous diseases at Berlin University. He performed pioneer work in the fight against alcoholism, and his views on the treatment of alkaloid addictions was fundamentally accurate. He also originated the doctrine of "exogenic reaction types."

Prof. Max de Crinis, erstwhile ordinarius in psychiatry at Cologne, has been appointed to succeed Professor Bonhoeffer. De Crinis is 49 years old. An Austrian by birth, he served formerly as extraordinary professor at the University of Graz, Austria. In 1934, after his Nazi sympathies had cost him his post in Graz, he was called to Cologne. He has worked on epilepsy and the histopathology of intoxications as well as on other histologic problems concerning nerve tissue.

Prof. Franz Volhard Has Retired

The professor of internal medicine at the University of Frankfort on the Main has been retired, having reached the age limit of active service, 68 years. A pupil of Riegel at Giessen, Volhard first served as senior physician in large hospitals at Dortmund and at Mannheim. In 1918 he became ordinarius in internal medicine at Halle on the Saale and in 1927 he assumed a similar post at Frankfort on the Main. His greatest contributions to internal medicine were above all in the field of gastric, circulatory and kidney disorders. In 1899 he discovered the lipolytic ferment of the stomach. He engaged in a vast amount of research on hypertonia, especially the interrelation of hypertonia and diseases of the circulation and the kidneys. Volhard has become best known for his work in the field of kidney diseases. One need only recall the Volhard specific gravity test of renal function. Volhard's treatise on Bright's disease, written in collaboration with Fahr, has enjoyed wide dissemination and recognition. The testing of renal function has been vastly improved and promoted by Volhard.

AUSTRALIA

(From Our Regular Correspondent)

Nov. 12, 1938.

The People and Socialized Medicine

After a hard fight and bitter contest, the labor government in New Zealand, despite the well organized campaign and extensive publicity of the nationalist opposition, has won a sweeping victory at the polls. At the last elections in 1935, labor came into office with a large majority, not because of its own policy but because it reaped the benefit of a popular reaction against the nationalist government. The main issue of the elections was the character and extent of social—or socialist—legislation. Mr. Savage took his stand on the social security act (in which provision is made for universal free medical service, increased pension allowances and unemployment insurance) and extended government control of banking policy. The opposition championed private enterprise against labor socialism, attacking the proposed extension of social services as financially unsound and advocating a more modest scheme of social benefits. In this it had the active support of the British Medical Association in New Zealand, which association indeed played a most active part in the election campaign. The people, however, have recorded a heavy vote in favor of state control. The official reaction of the medical profession to this position is uncertain. Before the elections the association in New Zealand had broken off all discussion with the government on health insurance matters, after the government's rejection of the association's proposals.

Law Relating to Abortion

The artificial interruption of pregnancy by a medical practitioner in a recent case of incest in South Australia has occasioned much discussion in medical and other circles as to the legal grounds for the termination of pregnancy after rape or incest. The law in this country is as follows: "Any person who, with intent to procure the miscarriage of any woman, whether she be or be not with child, unlawfully administers to her, or causes to be taken by her, any poison or other noxious thing, or unlawfully uses any instrument or other means whatsoever with the like intent shall be guilty of felony, and liable to imprisonment for life." The use of the word "unlawfully" implies that Parliament had in mind that such an act might be done "lawfully" if it was necessary to preserve the life of the mother, which in practice means her health and sanity, for, without either, life is worthless. The judge in the Bourne case in England, addressing the jury, said that it was obvious that the act if done by skilled persons without risk to the patient and on purpose to save the life of the mother must be lawful. The law did not permit the termination of pregnancy except for the purpose of preserving the life of the mother, but those words ought to be construed in a reasonable sense. If the physician was of the opinion, based on reasonable grounds and on adequate knowledge, that the continuance of pregnancy would probably make the woman a physical or mental wreck, the act was lawful. The law, however, does not permit the termination of pregnancy for humanitarian or eugenic reasons.

In the recent case of incest, the medical practitioner concerned brought the circumstances to the notice of the council of the South Australian Branch of the British Medical Association. After giving evidence in the police court that the girl was twenty-six weeks pregnant, he, who had been subpenaed, requested the magistrate to receive from him a recommendation to be forwarded to the branch council. In this it was recommended that, in consideration of the very grave doubt as to the future mentality of the child to be born and the danger to the future health and mental state of the child mother, physicians learned in such matters should confer with a view to ensuring nonsurvival of the infant. The council, however, has emphatically asserted in a public statement that it is not its province officially to advise members of the branch on the professional care of individual patients. It was pointed out to the practitioner concerned how the opinion of specialists might be obtained to determine whether the birth of the girl's child was fraught with danger to the life of the mother. No further action by the council was deemed necessary. Although it is realized by the council that public opinion is immensely and medical opinion is much in favor of the legal termination of pregnancy in cases of rape and incest, it has not yet considered what action, if any, should be taken in respect to alteration of the law concerning abortion.

Marriages

JOHN RICHARD HEATON, Hoopeston, Ill., to Miss Edyth Eleanor Clawson of La Fayette, Ind., October 29.

ROBERT A. HARE, Baltimore, to Miss Anne Lee Mead of Berkeley, Calif., in Alexandria, Va., October 23.

EUGENE LLOYD WENK, Cloutierville, La., to Miss Cammie Henry of Melrose in Alexandria, September 23.

ALFRED DEADERICK DOAK, Shelbyville, Ky., to Miss Evelyn Marie Cowan of Fayetteville, Tenn., in October.

LEWIS WILLIAM HAGNA, Marion, N. C., to Mrs. Evelyn Mentzer Innes of Huntington, Pa., in October.

JAMES GILBERT MASON WEYAND, Rochester, Pa., to Miss Susan Gallup of Beaver Falls, October 22.

RICHARD E. HOUSNER, Richland Center, Wis., to Miss Ardyce Kotvis of Hillsboro, October 30.

ROBERT WILLIAM BARRETT, Lexington, Mass., to Miss Alice Frances McNamara of Allston recently.

HERBERT PAUL DEXHEIMER, O'Fallon, Ill., to Miss Doris McGilligan at Tower Hill, October 29.

WILLIAM FREDRIC DELP to Miss Dorothy Elizabeth Wallner, both of Pulaski, Va., November 15.

DANTE PETER DAPOLONIA, New York, to Miss Buena Jones of West Point, Ga., September 30.

SAMUEL A. FREITAG to Miss Alice Elizabeth Kimball, both of Janesville, Wis., November 4.

ARTHUR ROWELL DAHLGREN, Atlanta, to Miss Jane Hartzog of Los Angeles, October 30.

WILLIAM R. BAKER to Miss Mary Corine Jaillet, both of Atlanta, Ga., in September.

OWEN C. CLARK, Oconomowoc, Wis., to Miss Grace Gasper of Waukesha, November 5.

LESTER J. BUIS, Pender, Neb., to Miss Isabel Connolly of Muncie, Ind., August 14.

GLENN S. EDGERTON, Hickory, N. C., to Miss Sylvia Steele of Statesville in October.

RALPH V. EVERLY, Indianapolis, to Miss Ruth L. Black of Brownstown, October 28.

LAWRENCE H. DONATH to Miss Mary Masters, both of Lake Geneva, Wis., October 1.

HENRY SARGENT HOWARD to Miss Louise Flora, both of Peoria, Ill., October 20.

GILBERT W. BENJAMIN, Baltimore, to Miss Doris Sundmacher at Radnor, Pa., recently.

CHARLES E. WALL to Miss Dorothy Burns, both of Manitowoc, Wis., October 8.

CLARK E. BAKER, Marion, Ill., to Miss Mary Rodd of St. Louis, September 10.

RAYMOND R. REMBOLT to Miss Mae Street, both of Lincoln, Neb., September 11.

GEORGE H. WEGMANN JR. to Miss Betty Sacia, both of Milwaukee, October 15.

RALPH VINJE to Miss Evangeline Kelley, both of Bismarck, N. D., October 27.

RALPH COHEN to Miss Paula Doris Josephie, both of New York, October 14.

TALCOTT BATES to Miss Margaret S. Pardee, both of New York, October 13.

SAMUEL BISHOP HUGHES, Wildwood, N. J., to Miss Anne Weber recently.

JOHN SEARLE GIFFIN to Miss Betty Burk, both of Waterloo, Iowa, October 8.

SIDNEY BERMAN to Miss Beatrice E. Kay, both of Detroit, October 22.

Deaths

James Allen Jackson ✠ Danville, Pa.; Jefferson Medical College of Philadelphia, 1906; Member of the House of Delegates of the American Medical Association, 1932-1937; fellow of the American College of Physicians; member of the American Psychiatric Association; teacher of neurology and psychiatry, Temple University School of Medicine, 1918-1920; superintendent of the Danville State Hospital; formerly associate editor of the *Atlantic Medical Journal;* editor of the *Mental Health Bulletin* published by the state hospital; in 1929 received the honorary degree of doctor of science from Bucknell University; aged 54; died, December 1, in the Jefferson Hospital, Philadelphia, of leukemia.

Sterling Newton Pierce ✠ Los Angeles; College of Physicians and Surgeons, Los Angeles, 1917; assistant clinical professor of obstetrics and gynecology, University of Southern California School of Medicine; member of the Pacific Coast Society of Obstetrics and Gynecology; fellow of the American College of Surgeons; on the staffs of the Cedars of Lebanon, Los Angeles General, California, Hollywood Clara Barton Memorial and the White Memorial hospitals; aged 51; died, September 30, of injuries received in an automobile accident.

Chauncey Vandever Umsted, Worcester, N. Y.; University of Pennsylvania Department of Medicine, Philadelphia, 1908; during the World War served as a member of an examining board; for many years deputy health commissioner in Yonkers; at one time visiting physician to St. Joseph's Hospital, Yonkers; aged 53; died, September 14, of heart disease and nephritis.

William Henry Chase, Montreal, Que., Canada; Dalhousie University Faculty of Medicine, Halifax, N. S., 1922; member of the American Association of Pathologists and Bacteriologists and the American Association of Neuropathologists; lecturer and Douglas Fellow in pathology at McGill University Faculty of Medicine and curator of the museum; aged 43; died, October 20.

Russell Ebenezer Atchison, Northville, Mich.; University of Michigan Homeopathic Medical School, Ann Arbor, 1900; member of the Michigan State Medical Society; for many years superintendent of the University of Michigan Homeopathic Hospital, Ann Arbor; aged 68; died, October 18, in the University of Michigan Hospital, Ann Arbor, of Parkinson's syndrome.

Glenn Levi Whiting ✠ Canisteo, N. Y.; University of Buffalo School of Medicine, 1904; past president of the Steuben County Medical Society; served during the World War; county coroner; member of the board of education; aged 62; on the staff of the Bethesda Hospital, Hornell, where he died, September 8, of bacillary dysentery and pernicious anemia.

Andrew Macphail, Montreal, Que., Canada; McGill University Faculty of Medicine, Montreal, 1891; formerly professor of the history of medicine at his alma mater and professor of pathology at the University of Bishop College Faculty; served during the World War; formerly editor of the *Canadian Medical Association Journal;* aged 73; died, September 23.

Stephen Thomas Quinn ✠ Elizabeth, N. J.; University of the City of New York Medical Department, 1897; fellow of the American College of Surgeons; on the staffs of St. Elizabeth's Hospital and Elizabeth General Hospital; served during the World War; aged 71; died, September 18, in the Sisters Hospital, Waterville, Maine, of bronchopneumonia.

Edgar Nathan Cowan, Merchantville, N. J.; Medico-Chirurgical College of Philadelphia, 1916; formerly assistant professor of biochemistry at the Medico-Chirurgical College, Graduate School of Medicine, University of Pennsylvania, Philadelphia; served during the World War; aged 58; died, October 24, of chronic nephritis and uremia.

Nathaniel Ross ✠ Wilkes-Barre, Pa.; Jefferson Medical College of Philadelphia, 1892; past president of the Luzerne County Medical Society; served during the World War; for many years physician to the school district; on the staff of the Nesbitt Memorial Hospital, Kingston; aged 71; died, September 24.

George McAlpin Liddell, Waco, Texas; Baylor University College of Medicine, Dallas, 1909; member of the State Medical Association of Texas; served during the World War; city health officer; on the staff of the Providence Hospital; aged 54; died, October 23, of injuries received in an automobile accident.

Frank Suggs, San Antonio, Texas; Arkansas Industrial University Medical Department, Little Rock, 1897; at one time member of the medical reserve corps of the U. S. Army; veteran of the Spanish-American and World wars; aged 63; died, September 10, of coronary occlusion and arteriosclerosis.

Edwin Aid Layton, Seattle; College of Physicians and Surgeons, School of Medicine of the University of Illinois, 1909; formerly medical missionary; for many years director of health of the public schools in Tacoma; aged 65; died, October 6, in the Emanuel Hospital, Portland, Ore., of myocarditis.

Charles W. Famous, Street, Md.; University of Maryland School of Medicine, Baltimore, 1901; member of the Medical and Chirurgical Faculty of Maryland; formerly member of the state legislature; aged 63; died, October 17, in the Union Memorial Hospital, Baltimore, of coronary thrombosis.

Emory Hamlin Wood, Salisbury Center, N. Y.; Hahnemann Medical College and Hospital, Chicago, 1881; member of the Medical Society of the State of New York; member of the board of education; for many years health officer; aged 78; died, September 18, of cerebral hemorrhage.

John William Funck ✠ Baltimore; University of Maryland School of Medicine, Baltimore, 1888; aged 84; for many years on the staffs of the Presbyterian, Eye, Ear and Throat Charity Hospital and the Franklin Square Hospital, where he died, October 4, of chronic myocarditis.

Orlando W. Brownback, Pendleton, Ind.; University of Pennsylvania Department of Medicine, Philadelphia, 1867; member of the Indiana State Medical Association; formerly health officer and member of the school board; aged 92; died, October 13, of chronic myocarditis.

Marcus White Fredrick, Brentwood, Calif.; Universität Leipzig Medizinische Fakultät, Saxony, Germany, 1888; member of the California Medical Association; formerly on the staff of the French Hospital, San Francisco; aged 77; died in September of chronic nephritis and uremia.

Vestal Raul Abraham ✠ Long Beach, Calif.; Rush Medical College, Chicago, 1913; fellow of the American College of Surgeons; served during the World War; on the staffs of the Long Beach Community, Seaside and St. Mary's Long Beach hospitals; aged 53; died in October.

Arthur Horace Gordon ✠ Chicago; Hahnemann Medical College and Hospital, Chicago, 1887; at one time professor of internal medicine at his alma mater; on the staffs of the Edgewater and Illinois Masonic hospitals; aged 75; died, December 2, of coronary thrombosis.

Jacob Clarence Kanigsberg ✠ Freeport, N. Y.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1926; on the staff of the Meadowbrook Hospital, Hempstead; aged 38; died, September 20, of cerebral embolism and aortic and mitral regurgitation.

Edward Albert Packard, Newton, Mass.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1886; member of the Massachusetts Medical Society; aged 80; died, September 8, in South Harpswell, Maine, of angina pectoris.

Frederick Henry Wetmore, Hampton, N. B., Canada; McGill University Faculty of Medicine, Montreal, Que., 1888; at various times had been health officer of Kings County, medical inspector of schools and coroner of Kings County; aged 76; died, September 30.

Olin Weston Daley, White River Junction, Vt.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1884; member of the Vermont State Medical Society; formerly member of the state legislature; aged 75; died, October 16.

Wendell Ambrose Jones, Riverside, Calif.; Ohio Medical University, Columbus, 1898; member of the California Medical Association; city and county health officer; served during the World War; aged 64; died, September 20, of cerebral hemorrhage.

John Lawrence Loftus, Old Forge, Pa.; Medico-Chirurgical College of Philadelphia, 1912; served during the World War; for many years member of the school board; on the staff of the Taylor Hospital, Scranton; aged 51; died, September 29.

Albert Hadley Cantril ✠ Portland, Ore.; Northwestern University Medical School, Chicago, 1902; fellow of the American College of Surgeons; aged 58; on the staff of the Emanuel Hospital, where he died, October 12, of cerebral hemorrhage.

Benjamin Franklin Lyon, Lancaster, Texas; University of Tennessee Medical Department, Nashville, Tenn., 1892; formerly bank president; aged 73; died, October 17, in the Dallas Medical and Surgical Clinic Hospital, Dallas, of bronchopneumonia.

Jones Houston Lamb ✠ Paragould, Ark.; Hospital College of Medicine, Louisville, Ky., 1905; past president of the Greene County Medical Society; member of the school board; aged 59; died, September 21, of carcinoma of the liver.

Edward Perry Clark, Los Angeles; Hahnemann Medical College and Hospital of Philadelphia, 1897; member of the California Medical Association; served during the World War; aged 64; died, September 5, of coronary disease.

Robert Blackburn Love, Livingston, Texas; Medical Department of Tulane University of Louisiana, New Orleans, 1900; member of the State Medical Association of Texas; aged 63; died in October of ruptured peptic ulcer.

Charles Pender Edwards, Asheville, N. C.; Tennessee Medical College, Knoxville, 1900; served during the World War; aged 63; died, October 6, in the Morton F. Plant Hospital, Clearwater, Fla., of cerebral hemorrhage.

Richard S. Bradley, Dalton, Ga.; Southern Medical College, Atlanta, 1884; member of the Medical Association of Georgia; aged 80; died, October 19, of acute dilatation of the heart and fractured neck of the femur due to a fall.

Chester C. Copelan ✠ Springfield, Ill.; Chicago College of Medicine and Surgery, 1915; served during the World War; aged 47; on the staff of St. John's Hospital, where he died, October 9, of splenic myelogenous leukemia.

Fisher F. Demuth, Cecil, Ohio; Eclectic Medical Institute, Cincinnati, 1882; formerly member of the state legislature; past president of the Paulding County Medical Society; aged 82; died, October 16, of cerebral thrombosis.

Conrad William Marxer ✠ Indianapolis; Central College of Physicians and Surgeons, Indianapolis, 1897; served during the World War; aged 66; died, October 15, in the Methodist Hospital of carcinoma of the sigmoid.

Herman John Wickman, Riverside, Calif.; State University of Iowa College of Medicine, Iowa City, 1906; member of the California Medical Association; aged 60; died, September 29, in the Riverside Community Hospital.

Charles G. Quammen, Mantorville, Minn.; Keokuk Medical College, College of Physicians and Surgeons, 1903; aged 64; died, September 11, at Rochester of typhoid and perforation of an ulcer of the ileum with peritonitis.

Edward W. Wahl, Los Angeles; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1890; served during the World War; aged 71; died, September 3, in a local hospital.

William Wallace Winans, Rochester, N. Y.; Hahnemann Medical College and Hospital, Philadelphia, 1899; aged 64; on the staff of the Highland Hospital, where he died, September 24, of coronary thrombosis.

Howard Andrew Lingenfelter, Durango, Colo.; University and Bellevue Hospital Medical College, New York, 1899; member of the Colorado State Medical Society; aged 66; died, October 23, of heart disease.

Earl Reuben Lee, Denver; Temple University School of Medicine, Philadelpia, 1932; member of the Colorado State Medical Society; aged 33; died, October 9, in the Fitzsimons Hospital of adenocarcinoma.

Claud E. Chandler, Mukilteo, Wash.; Willamette University Medical Department, Salem, Ore., 1908; member of the Washington State Medical Association; aged 55; died, October 12, in a hospital at Everett.

Louis Herbert Maxson, Seattle; University of Pennsylvania School of Medicine, Philadelphia, 1910; member of the American Society of Anesthetists; aged 55; died, October 3, in the Providence Hospital.

Alfred B. Wright, Buffalo; University of Buffalo School of Medicine, 1901; member of the Medical Society of the State of New York; aged 60; died, September 24, of cerebral hemorrhage and hypertension.

Edward Marcelis Clark, Mamaroneck, N. Y.; Bellevue Hospital Medical College, New York, 1885; member of the Medical Society of the State of New York; health officer; aged 76; died, September 10.

Walter P. Hailey, Haileyville, Okla.; Missouri Medical College, St. Louis, 1899; aged 62; died, September 12, in the Albert Pike Hospital, McAlester, of calcification of the pineal gland and angina pectoris.

Frederick Victor Lyman, Velva, N. D.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1903; aged 59; died, October 29, in a hospital at Minot of cerebral hemorrhage.

William Elmer Boyer, Newark, Ohio; Starling Medical College, Columbus, 1897; member of the Ohio State Medical Association; aged 68; died, October 4, of nephritis and Parkinson's disease.

Graham Lawrence, Shelbyville, Ky.; University of Louisville Medical Department, 1892; member of the Kentucky State Medical Association; aged 68; died, October 7, of cardiac thrombosis.

Alois J. Blickhan, Quincy, Ill.; Keokuk (Iowa) Medical College, 1891; member of the Illinois State Medical Society; aged 74; died, October 20, of arteriosclerosis and hypostatic pneumonia.

Frederick Richmond McBrien, Niagara Falls, N. Y.; Trinity Medical College, Toronto, Ont., Canada, 1891; aged 69; died, September 23, of uremia, pulmonary edema and nephritis.

Edward Hardaway Manson Parham, Lordsburg, N. M.; Medical Department of Tulane University of Louisiana, New Orleans, 1898; aged 61; died, September 10, of organic heart disease.

Frank Heywood Stocker, West Hartford, Conn.; New York Homeopathic Medical College and Hospital, 1897; aged 62; died, October 9, at the Hartford Hospital of lobar pneumonia.

James Roy Bierly ✠ Peoria, Ill.; Chicago College of Medicine and Surgery, 1911; served during the World War; aged 55; on the staff of the Proctor Hospital, where he died, October 18.

E. C. McComas, Flat Top, W. Va.; Tennessee Medical College, Knoxville, 1901; Maryland Medical College, Baltimore, 1904; aged 63; died, October 18, of acute dilatation of the heart.

Lealon Edward Lamb ✠ Clinton, Okla.; University of Oklahoma School of Medicine, Oklahoma City, 1928; aged 37; died, October 7, in the Menorah Hospital, Kansas City, Mo.

John Charles Stewart, Philadelphia; Hahnemann Medical College of Philadelphia, 1903; aged 54; died, September 16, of asphyxiation due to pressure from a deformity of the spine.

James Joseph P. Armstrong ✠ Douglas, Ariz.; Trinity Medical College, Toronto, Ont., Canada, 1893; aged 67; died, September 30, in La Jolla, Calif., of cerebral hemorrhage.

Alson David Ferris, Hardwick, Vt.; University of Vermont College of Medicine, Burlington, 1905; aged 71; on the staff of the Hardwick Hospital, where he died, October 5.

George R. Clayton Jr. ✠ La Fayette, Ind.; Illinois Medical College, Chicago, 1909; served during the World War; aged 54; died, October 17, of acute coronary thrombosis.

Elliott Vanveltner Converse, Palestine, Texas; Rush Medical College, Chicago, 1902; on the staff of the Missouri Pacific Lines Hospital; aged 59; died, October 8.

Henry Walter Lilly, Fayetteville, N. C.; Bellevue Hospital Medical College, New York, 1879; for many years bank president; aged 82; died, October 11, of myocarditis.

Wilson R. Cushing, Dublin, Va.; University of Maryland School of Medicine, Baltimore, 1881; member of the Medical Society of Virginia; aged 81; died, October 6.

Seth Marion Angle, Jackson, Mich.; Detroit College of Medicine, 1906; aged 64; died, October 4, in the W. A. Foote Memorial Hospital of intestinal obstruction.

Oshea Stowell Brigham ✠ Toledo, Ohio; Long Island College Hospital, Brooklyn, 1876; aged 86; died, October 16, of chronic myocarditis and acute bronchitis.

Otto Kothe ✠ Callicoon, N. Y.; University and Bellevue Hospital Medical College, New York, 1899; served during the World War; aged 61; died, September 27.

William B. Marks, Augusta, Ga.; University of Georgia Medical Department, Augusta, 1883; aged 76; died, October 11, of hypertension and coronary occlusion.

William H. Barkley, Cold Spring, Ind.; Cincinnati College of Medicine and Surgery, 1887; aged 82; died, October 24, of mitral stenosis and chronic prostatitis.

John B. Mahan, Cincinnati; University of Louisville (Ky.) Medical Department, 1889; aged 78; died in October of arteriosclerosis and cerebral hemorrhage.

Thomas Edmund Fitzgerald, Brooklyn; Cornell University Medical College, New York, 1904; died, September 10, in Cortland, N. Y.

Thomas D. Tharpe, Portsmouth, Va. (licensed in Virginia in 1908); aged 72; died, September 29, of coronary thrombosis.

Ernest McNeill, New York; Bellevue Hospital Medical College, New York, 1895; aged 66; died, September 6.

J. E. Sutton, Viola, Ark. (licensed in Arkansas in 1903); aged 69; died, September 21, of myocarditis.

Willis A. Clark, Cumby, Texas (licensed in Texas, under the Act of 1907); died, September 13.

Bureau of Investigation

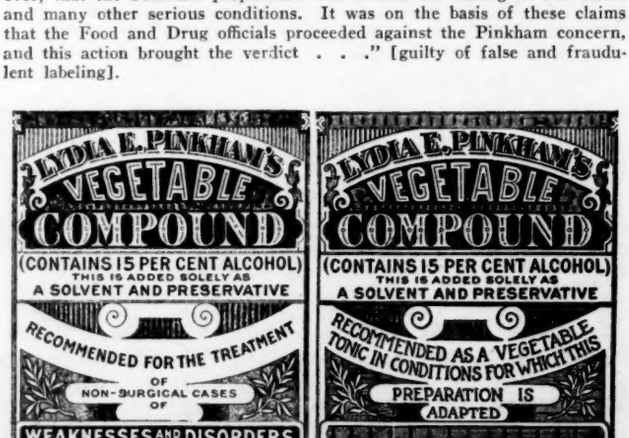
LYDIA E. PINKHAM'S VEGETABLE COMPOUND GETS ANOTHER NEW DRESS

The carton labels of "Lydia E. Pinkham's Vegetable Compound" have been modified many times as a result of the activities of the Food and Drugs Act of 1906 as amended, and subsequent citations in connection with its enforcement. The cuts (below) showing the labels which have appeared since 1900 are not new to the readers of THE JOURNAL. In an article by Dr. Arthur J. Cramp in *Hygeia* for November 1935 concerning this preparation, it was stated:

"It will be noted in the oldest label reproduced at the time that fraudulent statements on the trade package were merely immoral instead of illegal and potentially expensive—that Lydia Pinkham's Vegetable Compound was claiming to be 'A Sure Cure for Prolapsus Uteri or

NEW STYLE ADOPTED 1914
LYDIA E. PINKHAM'S
VEGETABLE
COMPOUND
A SURE CURE FOR
PROLAPSUS UTERI
OR FALLING OF THE WOMB
AND ALL
FEMALE WEAKNESSES
INCLUDING
LEUCORRHŒA, IRREGULAR AND PAINFUL
MENSTRUATION, INFLAMMATION AND ULCERATION
OF THE WOMB, FLOODING &c
FOR ALL WEAKNESSES OF THE GENERATIVE ORGANS OF EITHER SEX, IT IS SECOND TO NO REMEDY THAT HAS EVER BEEN BEFORE THE PUBLIC
LICAND FOR ALL DISEASES OF THE KIDNEYS IT IS THE
GREATEST REMEDY IN THE WORLD
LYDIA E. PINKHAM'S
VEGETABLE
COMPOUND
(CONTAINS 18 PER CENT ALCOHOL)
THIS IS ADDED SOLELY AS
A SOLVENT AND PRESERVATIVE
FOR
PROLAPSUS UTERI
OR FALLING OF THE WOMB
AND OTHER
FEMALE WEAKNESSES
INCLUDING
LEUCORRHŒA, IRREGULAR AND PAINFUL
MENSTRUATION INFLAMMATION AND ULCERATION
OF THE WOMB, &c
FOR WEAKNESSES OF THE GENERATIVE ORGANS, IT IS REGARDED AS SECOND TO NO OTHER REMEDY THAT HAS EVER BEEN BEFORE THE PUBLIC

Falling of the Womb, and All Female Weaknesses,' listing a number of interesting, if intimate, conditions. Following the passage of the law, the line on the label reading 'A Sure Cure for' was deleted, and the information that the law required, giving the amount of alcohol present (at that time 18 per cent), was declared. The label still implied, however, that the Pinkham preparation was a cure for falling of the womb and many other serious conditions. It was on the basis of these claims that the Food and Drug officials proceeded against the Pinkham concern, and this action brought the verdict . . ." [guilty of false and fraudulent labeling].



"Following this there was another change in the label, in which the stuff was 'Recommended for the Treatment of Non-Surgical Cases of Weaknesses and Disorders of the Female Generative Organs, Catarrhal Leucorrhea and Irritation.' About this time, also, the alcohol content was changed from 18 to 15 per cent. A little later the statement relative to 'Catarrhal Leucorrhea and Irritation' was deleted and yet another new label was issued. Then finally came the label that is being used today, in which it is stated that Lydia E. Pinkham's Vegetable Compound is 'Recommended as a Vegetable Tonic in Conditions for Which This Preparation is Adapted.' This statement is about as informative as it would be to say that 'For Those Who Like This Sort of Thing, This Is the Sort of Thing That Those People Like.'"

Now, according to an advertisement in the *American Druggist* for November 1938, the preparation has another new label. While it is still "Recommended as a Vegetable Tonic in Conditions for Which This Preparation is Adapted," if any, it is now called "Lydia E. Pinkham's Vegetable Compound (With Vitamin B_1)"—200 International Units to the Daily Dose. Just why this particular vitamin was selected by these old-timers in the "patent medicine" business is difficult to know.

Lydia E. Pinkham, of course, never heard of vitamin B_1. According to the Council on Pharmacy and Chemistry, vitamin B_1 is useful in correcting and preventing beriberi and anorexia of dietary origin in certain cases, and of value in securing optimal growth of infants and children, and is conceded to be a dietary essential which is of value in some conditions where difficulty in utilizing ordinary foods in the usual way is encountered. Since beriberi is only infrequently seen in the United States, and since the Pinkham preparation is obviously not for infants and children, it may be concluded that vitamin B_1 is added for correcting and preventing anorexia or to improve the utilization of ordinary foods where that utilization is not taking place. In view of many of the claims which have been used for the Pinkham preparation in the past, it is indeed surprising that the manufacturers, after deciding to add a vitamin, did not select vitamin E, since the latter vitamin, although not established, has been endowed with certain effects which were claimed for Lydia E. Pinkham's Vegetable Compound. How-

ADVERTISEMENT
MEN LOVE GIRLS WITH PEP
If you are peppy and full of fun, men will invite you to dances and parties.
BUT if you are cross, listless and tired, men won't be interested. Men don't like "quiet" girls. When they go to parties they want girls along who are full of pep.
So in case you need a good general system tonic, remember for 3 generations one woman has told another how to go "smiling thru" with Lydia E. Pinkham's Vegetable Compound. It helps build up more physical resistance and thus aids in giving you more pep and lessens distress from female functional disorders.
You'll find Pinkham's Compound WELL WORTH TRYING!

ever, there is no reason why the selection of the vitamin to be added to a nostrum of this type should be made on a rational basis.

The addition of vitamin B_1 to this old remedy is reminiscent of the change that was made in another nostrum many years ago. Quoting from THE JOURNAL for Sept. 28, 1912, it is stated in reference to "Peruna" that:

"In 1906 the Peruna company was notified that it either must put some medicine in its 'booze' or it could be sold only in saloons or other places carrying liquor licenses. The company thus found itself between the devil and the deep blue sea. If it left its nostrum as it was, it could only be sold by one who held a retail liquor dealer's license; this, of course, would at once make its real character evident to the purchaser. If, on the other hand, appreciable quantities of drugs were put into the stuff, it would spoil its sale as a beverage. Evidently believing that the preparation was so popular that nothing could hurt its sale materially, the company chose the latter course. A laxative was added and Peruna was still permitted to be sold as a medicine."

Peruna at that time contained about 20 per cent of alcohol. In 1920, however, this was reduced to 12 per cent, but in 1927 it was increased to 18 per cent and the senna was removed.

Changing formulas of "patent medicines" sold under the same name not infrequently causes considerable trouble to the user. Heavy users of Peruna probably did not appreciate its senna content. It must be granted, however, that there is probably nothing harmful in the addition of vitamin B_1 to Lydia Pinkham's Vegetable Compound. That there is any need for vitamin B_1 beyond that obtained in the normal diet, in any significant number of patients who take this "Compound," is something that is entirely unknown. It would be interesting to see exactly what type of claim is made by the manufacturer for this additional

ingredient. One is not able to determine this from the labels, since, as pointed out, the preparation is recommended in conditions for which it is adapted.

A current advertisement (cut above) may or may not refer in part or in toto to the new ingredient. Judging by this advertisement, vitamin B_1 may have been added for "tonic" effects, but a tablespoonful of the preparation, which has the alcoholic content of ordinary wine, may bring about certain "stepping-up" effects without the addition of any vitamin.

Another day, another label, a new age, a new ingredient, but still essentially the same old "female weakness" nostrum. Grandma used it and her daughter tolerated it, but her granddaughter should know better.

Correspondence

USELESS DUPLICATION IN TUBERCULOSIS WORK

To the Editor:—There is no other country in which there is more than one national tuberculosis association to combat tuberculosis in all its aspects and working in harmony with local societies, committees and specialistic organizations. Our country alone has the questionable distinction of having a number of so-called national bodies working and meeting independently of the National Tuberculosis Association. They include the American Clinical and Climatological Association, which meets annually and publishes its own transactions; the American Sanatorium Association, which meets at the same time as the National Tuberculosis Association and publishes its transactions with the latter's annual report; the Federation of American Sanatoria, which meets annually, and the American College of Chest Physicians and the American Academy of Tuberculosis Physicians, which meet also annually but like the former, independently of the meeting of the National Tuberculosis Association. The last three associations have for their official organ the monthly journal called *Diseases of the Chest.*

Before me is a letter dated Aug. 12, 1938, signed by the outgoing president, Ezra Bridge, and the incoming president, Bruce H. Douglas, of the American Sanatorium Association. In it there is first a suggestion for enlarged activities and members are asked to express their ideas concerning disbanding or enlarging and renaming the association. The letter concludes with the statement that the problem is now one of reorganization or amalgamation with the American College of Chest Physicians and the Academy of Tuberculosis Physicians. The Federation of American Sanatoria is not mentioned. The need of such a federation alongside the American Sanatorium Association, which has done such good work, is not apparent.

Why cannot all these activities be conducted under the auspices of the National Tuberculosis Association? The latter has a division for clinical section, administrative section, a pathologic section, a social work section, and so on. Nearly all phases of the tuberculosis problem except, perhaps, that of thoracic surgery are covered. This phase of phthisical therapy is so vast that there may be justification for the existence of an American Association for Thoracic Surgery, meeting separately and having its own monthly publications. Aside from that, one would think that the National Tuberculosis Association meets all the demands for considering in its program of work a complete tuberculosis therapy and prevention. Yet complaints have arisen: First, that the National Tuberculosis Association has neglected the western section of the country and particularly the interest of private sanatoriums; that the official organ of the society, the *American Review of Tuberculosis,* is too exclusive and inadequate to meet the demand for publication of many important papers on tuberculosis; that there is no criterion to judge competent specialists, and that the general practitioner has difficulty in selecting consultants when consultation is needed. To obviate the latter condition, a number of tuberculosis physicians in the western and some eastern parts of the country united to form the American College of Chest Physicians and the American Academy of Tuberculosis Physicians and create for their official organ a monthly journal entitled *Diseases of the Chest* and publish a directory of experienced pneumothorax physicians.

If all men treating a particular part of the body should unite under the name of an academy, would it not lead to confusion, particularly in large cities, where there is usually one good academy with sections for all specialties? How bewildering would such multiplicity of academies be to the general practitioner. In tuberculosis of the lung there are already two, and a large number of good specialists do not belong to either. Heretofore the general practitioner has seemingly had little difficulty in choosing the consultant in whom he had sufficient confidence. Yet, in view of the importance of having for the young general practitioner starting out in practice an authentic guide to consult when consultation in tuberculosis is needed, I venture to quote from the letter already mentioned as one aim of the American Sanatorium Association the following: "To encourage qualified members of the organization to apply for registration with the American Board of Internal Medicine of the American Medical Association, to further the establishment by the American Medical Association of special examination, certification and registration of specialists in tuberculosis under the auspices of the American Board of Internal Medicine." This is a spendid way to clarify and solve the problem. The only suggestion I would make here is to add that the qualified member should be an expert in pneumothorax and application of pneumolysis. This would do away with the need of the directory for pneumonthorax specialists. A list of consultants officially certified at the disposal of the general practitioner would be a guaranty of the competence of the consultant. While I have not the slightest doubt that the men who are members of the American College of Chest Physicians and the American Academy of Tuberculosis Physicians are equally competent as those who would pass the special examination qualifying as specialists in tuberculosis before the Board of Internal Medicine, membership in the two organizations created as a guaranty of qualification may not seem quite as secure to the young practitioner as the official list which the American Medical Association has at the disposal of inquirers.

The marvelous success in the reduction of the morbidity and mortality of tuberculosis was obtained prior to the past three years in which criticism, discontent and dissension among the workers arose. How great the result might be from united action of all the tuberculosis workers under the leadership of the officers and the Board of Directors of the National Tuberculosis Association, particularly since aided in their efforts by a benevolent United States government, the American Medical Association, the many state and local health departments, the equally numerous city and town tuberculosis associations and committees, the tuberculosis work of life insurance companies and, last but not least, all supported by an enlightened and generous public.

How very considerable a factor the United States government has already played in the antituberculosis crusade may be evident by a brief enumeration of its hospitals and sanatoriums. According to the latest Sanatorium Directory, the Veterans Administration Facilities for the care of the tuberculous ex-soldiers has no less than twenty-seven well equipped sanatoriums and all general hospitals operated by the administration have, besides, a few beds for observation and terminal cases. The U. S. Army and the U. S. Navy each has three tuberculosis hospitals; the U. S. Public Health Service operates seventeen tuberculosis hospitals and in addition to these there are six other U. S. Public Health Service hospitals which admit cases for observation and emergency care. For our Indians, our generous government has no less than fifteen sanatoriums

and thirteen general hospitals where tuberculous Indians are also admitted. Added to these government institutions the state, municipal and private sanatoriums throughout the country, we may proudly claim to have no less than 749 sanatoriums, preventoriums and general tuberculosis hospitals with a total capacity of 92,786 beds. In paying the just tribute to the splendid activities of our government, it is with equal pride that I state that no other body of civilian tuberculosis workers has achieved more success, has done more yeoman work in dealing with tuberculosis as a disease of the masses and to a very large degree is responsible for the marvelous mortality reduction of this disease than the National Tuberculosis Association.

The association elects a president every year and has a permanent secretary and treasurer. Hon. Franklin D. Roosevelt, President of the United States, is one of the association's honorary presidents. It has a board of directors of 101 which I would like to see increased by two representative physicians of the Negro race. Tuberculosis is still the medicosocial disease of the masses, attacking rich and poor alike, and among the colored population it is unfortunately most prevalent and with a seriously large morbidity and mortality. Much has been done and much is known but there is more to do and more to know.

In conclusion, I refer once more to that important letter addressed to all members of the American Sanatorium Association, which concludes as follows: "There is no doubt amalgamation of medical organizations in the tuberculosis field is desirable and that one organization of physicians interested directly and indirectly in tuberculosis should be the aim of all concerned."

S. ADOLPHUS KNOPF, M.D., New York.
16 West Ninety-Fifth Street.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

TESTING ENDOCRINE FUNCTIONING

To the Editor:—I should like to know about tests similar to the basal metabolic rate which indicate the normal or abnormal functioning of the endocrine glands, that is tests which determine normal or abnormal content of the various hormones of the pituitary, ovary and so on in such conditions as acne and menstrual disorders.

SOLOMON GREENBERG, M.D., Bayonne, N. J.

ANSWER.—The functional state of the endocrine glands can be determined in part by the following methods:

1. The amount of gonadotropic hormone in the blood and urine at the time of ovulation gives an estimate of the gonadotropic activity of the pituitary gland.

2. For the parathyroids by the fasting level of calcium and phosphorus in the blood.

3. For the pancreas by the fasting blood sugar content of the blood and by sugar tolerance tests.

4. The estrogenic content of the blood and urine during the menstrual cycle may give some indication of ovarian function. The chemical determination of urinary pregnandiol will reflect the activity of the corpus luteum.

5. For the testes by the amount of androgenic substance in the urine. In making these tests one can use any of the current methods described in any modern textbook of endocrinology (Werner, Lowenberg).

There is no pathognomonic hormonal picture associated with acne. Acne, however, is commonest at about the age of puberty. The condition is sometimes improved by the use of pituitary-like gonadotropic hormone extracts.

In all menstrual disorders it is advisable to eliminate nonendocrine factors such as debilitating diseases, blood dyscrasias and voluntary starvation for the purpose of reduction in weight. It is also important to eliminate organic lesions such as adrenocortical adenomas and pituitary adenomas.

In the absence of a nonendocrine factor or organic lesion of the endocrine glands, it is important to determine, if possible, which of the several endocrine glands is primarily responsible for the menstrual disorder. The thyroid function should be tested by means of the basal metabolism estimation and blood cholesterol.

A primary hypogonadism is determined by body measurements (relatively long extremities) and general appearance of the patient (boyish figure, usually underweight).

(*a*) The administration of gonadotropic substance is more effective in retarded puberty of boys with undeveloped sex organs.

(*b*) The postmenstrual state is characterized by the diminution or absence of estrogen and by an excess of the follicle stimulating hormone of the pituitary. Troublesome symptoms may be relieved by the prolonged administration of moderate doses of estrogen. This constitutes replacement therapy.

(*c*) Amenorrhea, secondary in character, if not caused by nonendocrine conditions or organic lesions of the pituitary, thyroid, adrenals or ovaries, may be overcome occasionally with low dosage irradiation of the pituitary gland and ovaries. When the uterus is hypoplastic, as it usually is in cases of amenorrhea, the administration of estrogen in large doses given intermittently is, sometimes, advisable for its stimulative effect on the muellerian tract.

(*d*) Menorrhagia may be controlled sometimes in those of child-bearing age by the administration of gonadotropic substance. In women at the menopause, menorrhagia may require a diagnostic curettage and the administration of radium. Progestin may be tried. It is usually ineffective.

It should be realized that the field of endocrine treatments in menstrual disorders is still largely in the stage of clinical investigation. Most menstrual disorders are best handled through the advice of a competent gynecologist.

PANCREATIC EXTRACT IN URETERAL STONE

To the Editor:—What results have there been from the use of pancreatic extract in the treatment of ureteral stones?

ROBERT S. MCCENEY, M.D., Laurel, Md.

ANSWER.—The efficacy of pancreatic tissue extract in the treatment of ureteral calculi remains in the experimental stage. The extract, which is the residual solution after insulin has been precipitated from pancreatic tissue, was first found to possess definite vasodilator properties. According to the opinion of most investigators (Frey: *München. med. Wchnschr.* **76**:1951, 1929; Gley: *Presse méd.* **27**:1279 [Oct.] 1929) the active agent is a hormone which is elaborated by and stored in the pancreas, passes into the blood in an inactive form, and is excreted in an active state in the urine. The so-called Frey hormone (Frey: *Ztschr. f. Biol.* **84**:321, 1926) is a substance which has been isolated from urine and has properties identical with those of pancreatic extract; in pancreatectomized animals the rate of urinary excretion of this hormone has been found to be reduced 80 per cent. Whether the hormone exerts its dilatory effect by neutralizing epinephrine or by balancing an overstimulation of the sympathetics remains a moot point. Villaret (*Presse méd.* **37**:633 [May] 1929), on the other hand, considers the physiologic activity of the extract due to sufficient amounts of choline, peptone and histamine which the hormone contains.

Because of its definite vasodilatory effects, Lazarus (*Urol. & Cutan. Rev.* **40**:847 [Dec.] 1936) studied the efficacy of the extract in cases of impassable ureteral calculi. He reports concerning its use in eight cases of impacted ureteral calculi and two cases of ureteral stricture with associated spasm. In all cases save one he was easily able to pass dilating catheters and bougies to the renal pelvis thirty minutes after one or two 1.5 cc. injections of the extract. While Lazarus administered the extract intramuscularly, it is noteworthy that Elliot (*J. Pharmacol. & Exper. Therap.* **43**:463 [Nov.] 1931) in animal experimentation found the extract to be active only when given intravenously and without effect when administered subcutaneously or intramuscularly.

Carrol (*South. M. J.* **31**:233 [March] 1938) advises a dosage of from 2 to 4 cc. given intramuscularly; he reports pain at the site of injection as a constant finding, but it lasts only a short time. Generalized reactions to the drug are minimal and those reported consist merely of faintness and vertigo. The extract has been found to be effective in the treatment of renal colic due to stone, in postcystoscopic colic, in the instrumental removal of calculi in the lower ureter, and finally in the treatments for dilation of organic ureteral stricture. Carrol states that the extract produces prompt relaxation of the ureters and has borne this out by experimental hydrophorographic tracings of the normal human ureter under influence of the drug.

CANCER OF BREAST

To the Editor:—A white woman aged 38 had a mass in the left breast removed. On biopsy and microscopic examination the mass was shown to be a highly malignant tumefaction composed of a cellular diffuse growth. The cells were unequal in size and shape; the nuclei were hyperchromatic and showed a large number of mitoses. The cytoplasm of the cells was either colorless or acidophilic. These cells were arranged in masses and columns and had a palisade formation. The desmoplasmic reaction was reduced to but a few strands of connective tissue. In the center of some of these cells were areas of mucoid degeneration. The diagnosis was duct carcinoma of the breast (grade 3, moderately radiosensitive). Should the entire breast be removed if no glands are present? Should radiation therapy be instituted before mastectomy? Would endocrine therapy aid the patient? What extension of life can be expected in this type of case? What is the prognosis? The x-ray report of the chest has not been received yet. The general physical condition and nutrition of the patient are good. The ears, nose, throat, heart, lungs, abdomen and extremities are normal. The blood pressure is 120 systolic, 80 diastolic. The blood count is within normal limits. The hemoglobin is 70 per cent, the red blood cell count 4,000,000 The patient has had three pregnancies going to full term and three miscarriages at two months. The blood Wassermann reaction is negative. The urine is normal. The mass was noticed in February 1938. After traumatic injury to the left breast the patient was operated on in August. The total mass measured 6.5 by 4.5 by 4 cm., covered by adipose tissue, and on cut section the mass was rather soft, was yellowish white, and had many chalky white pinpoints.

M.D., New York.

ANSWER.—It is evident from the record that the patient has a carcinoma of the breast. As she was operated on in August it is likely that further extension has occurred, as the tumor was removed locally even if there were no palpable nodes in the axilla. In about half the examples of carcinoma of the breast some involvement of the nodes is present, even though they are not palpable on physical examination. There is not the slightest advantage in preoperative irradiation, because any amount of radiation which can be given without serious damage to the healthy tissues will kill only a moderate percentage of the cancer cells and during the course of such preoperative irradiation further extension of the tumor into the breast tissues and the nodes is continuously taking place. A complete radical mastectomy should therefore be done immediately. After the wound is healed postoperative irradiation can be given. This increases the number of five year cures by about 10 per cent, provided the neoplasm has not already extended to the supraclavicular or mediastinal nodes; such a case is hopeless under any form of treatment. There is no evidence that any form of irradiation will completely sterilize diffuse carcinoma in the breast or in the axillary nodes; hence radical surgery at the present time is the only effective therapy of mammary carcinoma. This can be done with a cautery knife, electric spark or scalpel. There is some evidence that in advanced cases the use of the cautery or the cutting spark is preferable to scalpel surgery. In early carcinomas the scalpel method is just as effective as the others.

Endocrine therapy is useless. Prognosis is not possible in any individual case.

OBSCURE ATTACKS OF VERTIGO

To the Editor:—During the last two years I have seen six cases almost exactly alike. I have seen three of these six during the last month. Vertigo of rather sudden onset accompanied by nausea and vomiting is the only symptom. It is so severe that the patients fall down. Bed rest and sedation halt the nausea and vomiting but have little effect on the vertigo. In each case physical examination has failed to reveal any hint as to the cause. No disturbance in hearing was present and no abnormality of the external ear or ear drum could be found. The highest blood pressure in the group was 130 systolic; 80 diastolic. No obvious focal infection was demonstrable and no history of prevoius medication or illness was obtained. The duration of the disease varied from five to twelve days and no recurrences have been seen. I have been unable to arrive at a diagnosis other than labyrinthitis and since I am in general practice in a small town I am unable to account for the frequency of these cases. Any information on this point as well as a better diagnosis, etiology and treatment will be appreciated. Two females aged 11 and 50, and four males aged 9, 38, 40 and 60 were affected.

FORD F. KEPPEN, M.D., Three Oaks, Mich.

ANSWER.—Since all the patients recovered after a brief illness and there were no recurrences, the more serious organic lesions are obviously ruled out and the disturbance must be assigned to the vestibular system, including either the labyrinth or the vestibular branch of the eighth nerve. Many toxic substances and conditions, notably tobacco, alcohol, uremia and intestinal absorption, cause vertigo, partially at least through the effect on the labyrinth, so it is logical to assume that bacterial toxins can also produce a labyrinthitis. This is seen in encephalitis, in which, however, there may be neuritis as well as direct toxic action.

Israel S. Wechsler (A Text-Book of Clinical Neurology, ed. 2, Philadelphia, W. B. Saunders Company, 1931, p. 276) describes Gerlier's disease, an obscure condition in which vertigo is one of the principal symptoms. It is a rare disease occurring in certain areas of Europe as well as northern Japan, appearing only in the summer months, affecting mainly robust persons, coming in attacks which are repeated for a time and ultimately disappearing without recurrences. There are, however, usually ocular symptoms and muscular impairment.

The inquirer's description would fit certain prolonged migraine states were it not that they are single attacks. It therefore can probably be classed as a Ménière syndrome resulting from toxic labyrinthitis. In such attacks vertigo may be so severe that the patient clings to the side of the bed to remain in it or occasionally reports complete revolution of the bed or room.

Examination for nystagmus would be valuable and information as to the side to which the patients fall. Rotation tests, if suitable apparatus is available, would also be helpful.

RECURRENT STOMATITIS

To the Editor:—A male about 18 years of age has stomatitis caused by yeast hyphae—Leptotrichia buccalis. The canker sores occur in the tongue, and on the inside of the cheek and lips. They clear up for a time and then recur. He has had this condition for a long time. I have tried bismuth preparations, arsphenamine and silver nitrate without avail. Could you suggest some treatment which might be effective?

HAROLD F. HULBERT, M.D., Dansville, N. Y.

ANSWER.—Since the stomatitis has resisted local therapy and has repeatedly occurred after treatment, it would seem best to look for and correct an underlying condition. It is quite possible that the yeast organism is a saprophyte existing only because of a local decreased resistance.

It would be well to be sure that the Wassermann reaction is negative and that a pulmonary involvement does not exist in conjunction with the stomatitis.

Occasionally a change in the amount of gastric acidity will clear the mouth of local lesions. Test the fasting gastric contents for the degree of free acidity. If a hyperacidity or hypoacidity is present, give an appropriate alkali or acid in the usual form to counteract the abnormality.

If this simple therapy fails, obtain cultures of the dominant organisms in the stool and make a cutaneous test, using these antigens as well as one prepared from the mouth culture. Desensitization to the organisms producing positive cutaneous reactions may result in a changed susceptibility and healing of lesions in the gastrointestinal tract.

Other mouth washes than those named can be used, such as aqueous solutions of thymol (1 to 1,000) or solution of hydrogen peroxide from 1 to 4 per cent, which are sometimes effective.

TORTICOLLIS

To the Editor:—A Negro aged 44 complained that he "couldn't keep his face turned in front." He said that this condition had prevailed for four months. Examination showed that his chin stayed on the deltoid muscle of his left shoulder. He can turn his head and face forward only by using his hands. On removal of his hands it will snap back to the original position. There is one point of relaxation: when he drinks water, his head will stay quiet. The Wassermann reaction is negative; there is no deviation of the tongue, and eye convergence is normal. The patient neither smokes nor partakes of alcoholic beverages. All infected teeth have been removed. He gives evidence of perfect health otherwise. He has been receiving scopolamine hydrobromide one one-hundredth grain (0.00065 Gm.) for the last month triweekly. Please suggest treatment and references on this subject.

M.D., Missouri.

ANSWER.—The patient has a condition resembling a tonic torticollis or tic in which not only the right sternocleidomastoid muscle is at fault but the trapezius, splenius, scaleni and deep cervical muscles participate. Nearly all such cases are functional; that is, are not due to organic disease. They occur in persons who have a neuropathic diathesis. The fact that the patient's head will stay quiet when he drinks water indicates that there is no interference with function. There should be a complete neurologic examination to rule out any organic disease of the brain, spinal cord or cervical roots. If an organic lesion is present, one may do one of the operations described for that condition. Inquiry should be made in detail into the past history of the patient as well as with regard to the onset of the difficulty, because if a cause can be discovered the treatment must be directed to its removal. If no cause can be found, the following is suggested: Exercises in front of a mirror for five to ten minutes twice daily, the patient balancing a glass of water on top of his head; faradic current to the neck muscles on the left side of the patient once daily; supporting apparatus in the form of a pasteboard collar or a brace to be worn only in the daytime. Oppenheim's Textbook of Nervous Diseases, volume 2, is recommended for reference (pages 1246 to 1254).

DANGERS FROM PYRENE FIRE EXTINGUISHERS

To the Editor:—A pyrene fire extinguisher was used May 17 to put out a fire in a narrow hall in which the ventilation was poor. The fire was caused by a paperhanger's gasoline steamer, which was used to steam off the paper on the wall. The steamer caught fire and caused a blaze in an area measuring 3 by 4 feet. About a quart of pyrene was used. Immediately afterward my patient had difficult breathing, became cyanotic and had gastrointestinal disturbances such as flatulence and inability to digest food. These symptoms became worse about the tenth day. Cyanosis, labored respiration, flatulence, indigestion and a rapid pulse, 120, were noticed as well as a strong taste of pyrene. An area of about 4 cm. around the patient's anus was red and inflamed. Supportive treatments such as digitalis, glyceryl trinitrate and strychnine were used with liquid and soft diet. Aromatic spirit of ammonia was used for the difficult respiration, this proving the most satisfactory stimulant. Four weeks later the patient noticed that the maxillary and ethmoid cells were blocked. When these were opened and drainage established, a taste and smell of pyrene were again noticed with a recurrence of symptoms. They subsided and the patient felt better. July 12 he took some sodium phosphate for constipation and again had a recurrence of symptoms, especially the difficult breathing, which is most noticeable at night. A roentgenogram was taken of the chest. The heart is normal in size; there is some infiltration about the hili of the lungs but this has been present for years. Now the patient's pulse is normal but he still has some difficulty in breathing at night and some cyanosis. What effect would pyrene mixed with gasoline have on the organs and structures of the body? What chemistry is involved in this condition? What change if any should be instituted in the therapy? G. J. SEARLE, M.D., Mansfield, Ohio.

ANSWER.—It appears probable that under the influence of heat the carbon tetrachloride of the pyrene was in part decomposed into phosgene. As little as 4 parts of phosgene per million of air may be injurious. The reason for the greater toxicity of phosgene over hydrochloric acid is probably that phosgene is absorbed as such and the toxic effects are relatively slight in the upper air passages where there is little moisture. The effect reaches its maximum in the alveoli, where the moisture content is much higher and the liberated hydrochloric acid causes corrosion. This probably explains the greater toxicity of phosgene as compared with comparable amounts of hydrochloric acid. Ordinarily phosgene action is delayed for a few hours but it may appear immediately. Its chief action leads to pulmonary edema and cyanosis. Ordinarily these manifestations are associated with a sense of constriction of the chest, coughing, nausea and vomiting. Pneumonia may appear and occasionally lung abscesses. Few patients die if they survive the first three days and escape serious sequels.

In the present instance the development of the sinusitis is undoubtedly on an infectious basis. At this late time there is no treatment with reference to the specific cause. At the outset of this type of case the patient should be placed absolutely at rest and given oxygen inhalation, and external heat should be applied. The use of digitalis as was administered in this case is commendable. The irritating cough should be diminished through the use of usual types of respiratory sedatives.

In this accident there is little reason to believe that any combination took place between escaping gasoline and carbon tetrachloride. Recurring taste of pyrene is believed to be unimportant, as little if any of this substance is retained in the nasal cavities. This type of accident is prone to provoke neuroses, but in this instance they should be dispelled through the knowledge that there is reasonable assurance that complete recovery will take place and within a short period. See also Queries and Minor Notes in THE JOURNAL, July 30, 1938, page 469.

HYPERTONIC DEXTROSE SOLUTION IN PULMONARY EDEMA

To the Editor:—At this hospital it is almost a routine practice to administer hypertonic dextrose (50 cc. of 50 per cent solution) intravenously in the treatment of acute pulmonary edema and of right heart failure. No one has thus far been able to give me a satisfactory physiologic explanation for its use, nor have I been particularly impressed clinically by its results either alone or in conjunction with other methods. Is there a rationale behind this treatment or am I right in asserting that it is actually deleterious in that it throws an additional burden on an already overloaded circulation? M.D., New York.

ANSWER.—The administration of hypertonic dextrose solution intravenously in pulmonary edema and in failure of the right side of the heart is of certain value in some cases. The hypertonic solution takes up water from the tissues and may take enough fluid from the lungs to cause a symptomatic improvement. With normal kidney function and normal volume of blood flow through the kidneys the fluid taken up is excreted promptly and there is no increase in blood volume provided it is not given too rapidly. In cases of impaired kidney function it is always possible that there may be an increase in blood volume and that the increased blood volume might force an additional load on the heart. The additional dextrose content is supposed to be of value to the heart muscle, although under ordinary conditions it is probable that sufficient dextrose is being supplied normally.

As in the case of other therapeutic procedures which are effective, the administration of a hypertonic solution of dextrose may do harm as well as good and the indications and contraindications for its use must be carefully weighed in each individual case. When the edema is paroxysmal and due to a temporary coronary insufficiency, for example, it may be of value. In coronary occlusion with an infarcted heart muscle the increased blood volume might do harm.

X-RAYS CONTRAINDICATED FOR CARCINOMA OF LIVER

To the Editor:—A man aged 52 had five successive typical stone in the common duct gallbladder attacks the first week in August 1938 preceded by two weeks of progressive jaundice. September 8 a primary adenocarcinoma of the gallbladder and its duct with metastases to the surface of the right lobe of the liver was revealed at operation; the metastatic liver area was about 3 by 4 inches. Freeing of some two adhesions from the gallbladder duct produced a flow of bile with decided decrease in itching and an increase in appetite, but it is doubtful whether it will last. Could high voltage roentgen therapy be used here with advantage, offsetting the possible liver damage? Further operative procedures are, of course, out of the question, even drainage of the gallbladder which was so far below and back that a drain would kink. Is there any specific for the itching in severe jaundice? I have tried about everything but would appreciate any suggestions. Do you know of any two or three "appetizers" for carcinoma patients? One other complaint is that everything tastes sweet, even the water. M.D., Ill.

ANSWER.—Roentgen therapy is of no value in the treatment of either cancer of the gallbladder or cancer of the liver. This procedure is definitely contraindicated in the treatment of cancer of the liver. There are no specific therapeutic agents for the relief of itching in severe jaundice. There are no appetizers which are specially useful for carcinoma patients.

UNUNITED FRACTURE AND SYPHILIS

To the Editor:—An unmarried white man aged 28 consulted me six months ago for treatment of a recently fractured toe (metatarsal bone). The toe was slow to heal and even now the fracture line is still clearly seen transversely through the middle third of the bone. Some callus is naturally present but calcification is not complete. The delayed union led me to suspect latent syphilis. The patient admitted that in 1935 he had three rather painless lesions on the penis for which he sought medical advice. He was sent to a laboratory for smears which he believes were reported negative; nevertheless he was given nine "shots" of an intravenous preparation but no more thereafter and no other treatment. A Wassermann test made recently was negative. Because he complained of visual disturbance he was referred to an ophthalmologist, who noted an inequality in the size of the pupils, which reacted slowly to light; a choroiditis was reported. On receiving this report I made a spinal puncture and found the fluid clear and not under increased pressure. The cell count was from two to three cells with a slight trace of globulin. The Wassermann test was negative but the colloidal gold curve was 0003330000. What is your interpretation of these observations? Do you think antisyphilitic treatment is indicated? If so, would you recommend tryparsamide in view of the eye examination? M.D., California.

ANSWER.—There is no clear relationship between ununited fracture and syphilis. The most recent detailed orthopedic studies indicate that syphilis is in relatively uncommon association with ununited fracture and that nonunion is much more often due to other causes. It is, however, undeniable that in a few instances syphilis may be concerned in the causation of nonunion of fracture.

The history of penile sores in 1935 is only suggestive of the diagnosis of syphilis and is by no means certain. About 50 per cent of all penile sores are syphilitic; the other 50 per cent are not syphilitic in character. This particular patient was treated on suspicion for early syphilis without a definite dark field or serologic diagnosis, and it is by no means certain from the history given that the nine "shots" were actually treatment for syphilis or were some other type of medication.

The ophthalmologic abnormalities recently discovered are also not diagnostic of syphilis. The slight inequality of the size of the pupils and the sluggish light reaction may be found in normal persons. Choroiditis may of course occur as a result of many causes of which syphilis is only one.

The abnormal colloidal gold curve cannot be definitely interpreted in view of the fact that the spinal fluid was otherwise normal. The particular reading of the gold curve reported suggests that this may be laboratory error.

On the basis of the facts given, no conclusion can be reached as to whether the patient does or does not have syphilis. The desirability of treatment and the type of treatment, if any is to be given, could be determined only after competent syphilologic consultation.

IDIOSYNCRASY TO ATROPINE EYE DROPS

To the Editor:—To a girl in good health I gave 2 grains (0.13 Gm.) of atropine sulfate in one-half ounce (15 cc.) of water. Directions were to drop one drop in each eye three times a day. Her eyes were crossing at times and I wanted to refract them. Two hours later she returned after using a drop in each eye. She was in a state of excitement with griping in the abdomen, bowel movement, pain in the legs, temperature about 103 F., headache, and flushing of the skin over the entire body. This seemed like a typical poisoning. Is there any specific treatment? Would these symptoms occur if I used homatropine hydrobromide in her eyes for a refraction?

M.D., Texas.

ANSWER.—The solution of atropine sulfate used was somewhat less than 1 per cent, which is the usual strength employed to cause paralysis of the ciliary body preceding refraction. The patient used two drops, which contained about 0.001 Gm. of atropine sulfate. The condition following this instillation was typical of atropine poisoning.

Idiosyncrasy to atropine is frequent and small doses may produce distressing and alarming symptoms. The fatal dose is relatively large, so that, although poisoning from atropine is fairly frequent, deaths from atropine are quite rare. As little as 0.1 mg. (1/650 grain) may cause symptoms of atropine poisoning in susceptible persons. The smallest fatal dose is recorded as 130 mg. (2 grains), given by mouth.

Atropine poisoning may be treated by giving a solution of tannic acid or, lacking this, a strong infusion of tea leaves. Pilocarpine hydrochloride in 0.01 Gm. (one-sixth grain) doses may be tried. This is repeated if necessary until the mouth is moist. Small doses of morphine sulfate may be given cautiously for excitement; for depression, if present, caffeine may be given.

Homatropine hydrobromide in amounts that would be used for ciliary paralysis does not induce systemic poisoning nor is there the tendency to produce or aggravate a condition of glaucoma, since the paralysis is of so much briefer duration. Homatropine does not produce delirium or mental excitement.

MENSTRUATION AND FOOD SPOILAGE

To the Editor:—It seems to be generally agreed in this locality that if women do canning, especially that part of canning concerned with the pickling of foods, while they are menstruating, the food will later spoil. I have been asked for an explanation for this phenomenon and, having never heard of it myself before, I could think of no logical reason. Is this simply an erroneous belief concerned with the old superstitions surrounding menstruation or is there actually truth in it? I would appreciate any information you might be able to furnish me either to confirm or deny this belief.

M.D., Ohio.

ANSWER.—The inquirer may be referred to the first chapter in "Menstruation and Its Disorders" by Novak or to the monumental work of Ploss "Das Weib."

As is well known, there have been and still are many superstitious and erroneous ideas concerning the menstruating woman and the menstrual flow. Among others is evidently the one that the menstruating woman or the menstrual flow will in some way spoil food. There is no scientific basis for such a belief, and so far as actual scientific study is concerned there is apparently none mentioned in the literature.

DIABETES INSIPIDUS

To the Editor:—A girl about 18 years of age with diabetes insipidus has absolutely no complaints beyond frequency of urination, day and night, and her urgent desire for water. I have not been able to find any other trouble in either the physical or the laboratory examination. A roentgenogram of the sella turcica reveals no abnormality there. She responds to the injection of solution of posterior pituitary and also of pitressin. Before such treatment was instituted she found that she had to get up at night about twelve times, so that her rest and sleep were much disturbed. Now, while she has been under observation and taking either solution of posterior pituitary or pitressin once a day, she gets up about twice a night. Is it advisable to give the patient a hypodermic and allow her to administer pitressin to herself at home every night?

D. A. MACGREGOR, M.D., Wheeling, W. Va.

ANSWER.—A spinal puncture can sometimes be made in early cases of diabetes insipidus, primarily for diagnostic purposes but also because the occasional condition may be immediately and sometimes permanently relieved by the withdrawal of from 10 to 20 cc. of spinal fluid. The results of injection of solution of posterior pituitary are satisfactory in most cases, but such treatment has disadvantages. Disagreeable side effects are provoked, such as pallor, headache, palpitation and diarrhea. Also, the material is expensive, and if the services of a physician or nurse are required to give the frequent injections necessary the cost may be prohibitive. Patients with diabetes mellitus customarily are trained to inject themselves with insulin, and few accidents have resulted. Solution of posterior pituitary, however, like solution of epinephrine, because of local vasoconstrictor action, is less safe to place in the hands of laymen for subcutaneous use. Anaerobic bacteria, spores of tetanus and those of gas-forming organisms, if accidentally introduced beneath the skin in a region rendered ischemic by vasoconstriction, theoretically would be more dangerous, and in practice more accidental infection has occurred from injection of vasoconstricting substances than from insulin. These objections are avoided by the administration of dry, powdered substance of the posterior lobe intranasally (Smith, F. M.: Diabetes Insipidus, Treatment by Intranasal Insufflation of Posterior Lobe Pituitary Powder, THE JOURNAL [March 3] 1934, page 660), which in most cases, if repeated at sufficiently frequent intervals, is as effective as any other method of administration of pituitary.

VASODILATORS AND HEADACHE

To the Editor:—A woman aged 56 has hypertension with evidence of coronary sclerosis. She has had persistent headaches since puberty, relieved only by hot showers directly on the head and by hot applications to the head. This headache is always aggravated by vasodilators, which have been prescribed for her from time to time. It seems that vasodilators do not exercise a selective action in this case. Since she is not a patient of mine, I do not know of any other facts. She has been treated for a long time without beneficial results. I should like to know about any similar cases and whether there is anything one might do to relieve the precordial pain without aggravating the headache and vice versa.

M.D., New York.

ANSWER.—It is not possible to be explicit with the data at hand. The effect of vasodilator drugs in causing headaches in normal persons is well known. The headache accompanying the administration of glycerol trinitrate is an example. Some cases of chronic headache might reasonably be supposed to be aggravated by such drugs. The consequent fall in blood pressure might also be a factor.

If the more rapidly acting nitrites cannot be used for the acute paroxysms of cardiac pain, the effect of spirituous liquors might be tried or strong black coffee.

For constant use between the attacks, one of the purine base diuretics might be tried, for example one of the theobromines. They produce a definite coronary vasodilator effect with minimal peripheral vasodilatation.

IONTOPHORESIS

To the Editor:—Please give me information regarding the deposit of metals or metallic solutions in the skin by electrolysis. I am not referring to the deposit of such metals by the use of the needle but by the diffuse action of such metals. I should appreciate details of the amount of current necessary, the apparatus to be used, and so on.

M.D., California.

ANSWER.—It is doubtful whether metals can be transported across and deposited in tissues of appreciable thickness. Little more than surface deposits can be expected. There is considerable controversy on this matter in the voluminous literature, but proponents for iontophoresis have by no means presented solid, convincing evidence for the exaggerated claims which many of them make. For details of this method the inquirer is referred to the following:

Kovacs, Richard: Electrotherapy and Light Therapy, Philadelphia, Lea & Febiger, 1938.

Hollander, A. R.: Physical Therapeutic Methods in Otolaryngology, St. Louis, C. V. Mosby Company, 1937.

The Interrupted Low Frequency and the Constant Electric Current in Medicine, Report of the Council on Physical Therapy, THE JOURNAL, Oct. 31, 1936, p. 1469.

LYMPHOSARCOMA

To the Editor:—I received the following report on a gland removed from the supraclavicular area. What is the prognosis and what is the best treatment for this condition? There are no metastases and the patient's general condition is excellent. This is of approximately two months' duration. Microscopic examination: The normal architecture of the lymph node is almost completely replaced by diffuse hyperplasia of atypical lymphoblasts. There are infiltrations of lymphoblasts through the capsule into the surrounding fat tissue. There are occasional eosinophils, but the absence of myeloid giant cells and fibroblasts would indicate lymphoblastoma rather than Hodgkin's disease.

M.D., Ohio.

ANSWER.—The treatment for lymphosarcoma is either by x-rays or by radium. The prognosis depends on the extent of the disease and the efficiency of the treatment. When adequate radiation therapy is administered to a localized area of lymphosarcoma there is an excellent chance of complete sterilization of the treated focus. The bad prognosis usually associated with this disease is due to the fact that there frequently exist outlying areas which are affected by the disease but which are clinically not recognizable.

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BOARDS

Examinations of state and territorial boards were published in THE JOURNAL, December 10, page 2235.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II. Medical centers having five or more candidates desiring to take the examination, Feb. 13-15, May 1-2 (Part II only—limited to a few centers), June 19-21, and Sept. 11-13. Ex. Sec., Mr. Everett S. Elwood, 225 S. 15th Street, Philadelphia.

SPECIAL BOARDS

AMERICAN BOARD OF ANESTHESIOLOGY: An Affiliate of the American Board of Surgery. Written examination, Part I, will be held in various cities of the United States and Canada, April 8. Oral examinations for all candidates, St. Louis, May 13-14. Applications must be filed not later than sixty days prior to the date of the examinations. Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York.

AMERICAN BOARD OF INTERNAL MEDICINE: Written examinations will be held in various parts of the United States, Feb. 20. Application must be received on or before Jan. 1. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: General oral, clinical and pathological examinations for all candidates, Part II examinations, (Groups A and B) will be held in St. Louis, May 15-16. Application for admission to Group A examinations must be on file in the Secretary's office by March 15. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh (6).

AMERICAN BOARD OF OPHTHALMOLOGY: St. Louis, May 15. Applications must be filed before February 15. Sec., Dr. John Green, 3720 Washington Blvd., St. Louis.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: Memphis, Tenn., Jan. 13-14. Sec., Dr. Fremont A. Chandler, 6 N. Michigan Ave., Chicago.

AMERICAN BOARD OF OTOLARYNGOLOGY: St. Louis, May 12-13 and Chicago, Oct. 6-7. Sec., Dr. W. P. Wherry, 1500 Medical Arts Bldg., Omaha.

AMERICAN BOARD OF PATHOLOGY: Richmond, Va., April 8-9. Sec., Dr. F. W. Hartman, Henry Ford Hospital, Detroit.

AMERICAN BOARD OF PEDIATRICS: New York, April 26. Appointments must be made before Dec. 26. St. Louis, May 16. Appointments must be made before Jan. 16. Cincinnati, Nov. 14-15. Appointments must be made before July 14. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York, Dec. 28-30. Sec., Dr. Walter Freeman, 1028 Connecticut Ave. N.W., Washington, D. C.

AMERICAN BOARD OF RADIOLOGY: St. Louis, May 11-14. Sec., Dr. Byrl R. Kirklin, 102-110 Second Ave. S.W., Rochester, Minn.

AMERICAN BOARD OF UROLOGY: New York, Jan. 13-15. Sec., Dr. Gilbert J. Thomas, 1009 Nicollet Ave., Minneapolis.

California July Examination

Dr. Charles B. Pinkham, secretary, California State Board of Medical Examiners, reports the written examination held at Los Angeles, July 12-14, 1938. The examination covered nine subjects and included ninety questions. An average of 75 per cent was required to pass. One hundred and twenty-eight candidates were examined, 120 of whom passed and eight failed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
College of Medical Evangelists	(1935) (1936) 80.2, (1937) 80.4, 81.4, 83.3, (1938) 75.6, 76.2, 78.2, 78.2, 78.2, 78.8, 79, 79.2, 79.2, 79.3, 79.6, 80, 80.6, 80.7, 80.9, 81.1, 81.3, 81.4, 82.1, 82.2, 82.8, 82.8, 83, 83, 83.1, 83.2, 83.3, 83.4, 83.6, 83.7, 83.8, 84.3, 84.3, 85.2, 85.6, 85.6, 86, 86.3, 87.7		76.4,
Stanford University School of of Medicine	(1938) 85, 86.3, 86.3		82.9,
University of California Medical School	(1937) 87.2, (1938) 83.2, 84.7, 85.6, 85.8		76.1,
University of Southern California School of Medicine	(1938) 78.2, 78.6, 79.7, 79.9, 83.3, 84.4, 84.4, 84.6, 84.7, 84.8, 84.9, 85.2, 85.6, 85.9, 86.3, 86.4, 86.8, 86.9, 87, 87.2, 87.6, 87.6, 87.8, 88.7, 89.2		77.1,
George Washington University School of Medicine	(1937)		79.9
Georgetown University School of Medicine	(1937)		77.2
Loyola University School of Medicine	(1930) (1938) 80.2, 83.9		80.2,
Northwestern University Medical School	(1937)		85.2,
Rush Medical College	(1938) 81.7, 82.8		
University of Illinois College of Medicine	(1937)	77,	86.2
State University of Iowa College of Medicine	(1938)		80.7,
University of Kansas School of Medicine	(1932)		83.8
University of Louisville School of Medicine	(1937)		77.4
Tulane University of Louisiana School of Medicine	(1938)		79.3
Harvard University Medical School	(1937)		77.8
University of Michigan Medical School	(1935) 84.9, (1937)		86.4
Wayne University College of Medicine	(1936)		78.9
St. Louis University School of Medicine	(1938)		81.8
Creighton University School of Medicine	(1937) 80.1,		81.8
University of Nebraska College of Medicine	(1937) 81, (1938)		75
Woman's Medical College of Pennsylvania	(1937)		83.7
Vanderbilt University School of Medicine	(1936)		78.4
Baylor University College of Medicine	(1937)		87.4
McGill University Faculty of Medicine	(1937) 81.3,		84.9
Deutsche Universität Medizinische Fakultät, Prag	(1937) 77.9, 81.6,		84.1
Université de Paris Faculté de Médecine	(1932)		80
Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin	(1929)		77.9
Hessische Ludwigs-Universität Medizinische Fakultät, Giessen	(1920) 78.9, (1926)		84.8
Thüringische Landesuniversitat Medizinische Fakultät, Jena	(1927)		78.8
	(1920)		82.2

School	FAILED	Year Grad.	Per Cent
Stanford University School of Medicine	(1936)		63.3
Northwestern University Medical School	(1938)		70.7
Creighton University School of Medicine	(1936) 66.6, (1937)		74.4
University of Nebraska College of Medicine	(1935)		72.1
Duke University School of Medicine	(1936)		74.2
University of Oklahoma School of Medicine	(1937)		67.8
Universität Köln Medizinische Fakultät	(1921)		70.7

Indiana June Examination

Dr. J. W. Bowers, secretary, Indiana State Board of Medical Registration and Examination, reports the written examination held at Indianapolis, June 22-24, 1938. The examination covered fifteen subjects and included 100 questions. An average of 75 per cent was required to pass. One hundred and nine candidates were examined, 108 of whom passed and one failed. The following schools were represented:

School	PASSED	Year Grad.	Number Passed
Loyola University School of Medicine	(1938, 2)*		2
Northwestern University Medical School	(1938, 2)		2
Rush Medical College	(1937), (1938)		2
School of Med. of the Division of Biological Sciences	(1937)		1
University of Illinois College of Medicine	(1938, 3)		3
Indiana University School of Medicine	(1937), (1938, 77)		78
Indiana University School of Medicine			4†
University of Louisville School of Medicine	(1938, 2)		2
Johns Hopkins University School of Medicine	(1935), (1938)		2
Harvard University Medical School	(1937)		1
University of Minnesota Medical School	(1927)		1
St. Louis University School of Medicine	(1937)		1
Jefferson Medical College of Philadelphia	(1935)		1
McGill University Faculty of Medicine	(1934), (1938)		2
Albertus-Universität Medizinische Fakultät, Königsberg	(1925)		1
Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin	(1934), (1937)		2
Ludwig-Maximilians-Universität Medizinische Fakultät, München	(1936)		1
Universität Heidelberg Medizinische Fakultät	(1914)		1
Magyar Királyi Pázmány Petrus Tudományegyetem Orvosi Fakultasa, Budapest	(1926)		1

School	FAILED	Year Grad.	Number Failed
Rheinische Friedrich-Wilhelms-Universität Medizinische Fakultät, Bonn	(1937)		1

* These applicants have completed the medical course and will receive the M.D. degree on completion of internship. Licenses have not been issued.

† These applicants will be granted licenses on presentation of diploma.

Nevada Reciprocity Report

Dr. John E. Worden, secretary, Nevada State Board of Medical Examiners, reports three physicians licensed by reciprocity after an oral examination on Aug. 1, 1938. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Kentucky School of Medicine	(1902)		Montana
University of Minnesota Medical School	(1938)		Minnesota
University of Buffalo School of Medicine	(1918)		New York

New Mexico October Report

Dr. Le Grand Ward, secretary, New Mexico State Board of Medical Examiners, reports the written examination held at Santa Fe, Oct. 10-11, 1938. The examination covered thirteen subjects and included ninety questions. An average of 70 per cent was required to pass. One candidate was examined and passed. Fourteen physicians were licensed by endorsement from August 29 through November 3. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Rush Medical College	(1937)		90.3

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
College of Medical Evangelists	(1916)		California
University of Colorado School of Medicine	(1934)	N. B. M. Ex.	
Emory University School of Medicine	(1930)		Florida
Chicago Medical School	(1935)		Illinois
University of Kansas School of Medicine	(1936)		Kansas
University of Louisville Medical Department	(1916), (1919)		Kentucky
University of Louisville School of Medicine	(1924)		Kentucky
Nebraska School of Medicine	(1899)		Wyoming
University of Buffalo School of Medicine	(1934)	N. B. M. Ex.	
Baylor University College of Medicine	(1933)		Texas
University of Texas School of Medicine	(1937, 2)		Texas
University of Wisconsin Medical School	(1929)		Wisconsin

Book Notices

The Heart in Pregnancy. By Julius Jensen, Ph.D. (in Medicine), M.R.C.S., L.R.C.P., Assistant Professor of Clinical Medicine, Washington University School of Medicine, St. Louis. Cloth. Price, $5.50. Pp. 371, with 5 illustrations. St. Louis: C. V. Mosby Company, 1938.

This volume represents a critical survey of the literature and present day thought on heart disease and its relation to problems of reproduction. Cardiac disease is probably the most frequent accidental complication of pregnancy and accounts for about 7 per cent of maternal deaths. Improved antepartum care has greatly reduced the death rate. The improved prognosis for the patient with cardiac disease during pregnancy has been made possible by cooperative study and care of the patient by a competent internist and an obstetrician. The author, who is an internist, has had the exceptional opportunity of studying a large group of patients with cardiac disease in cooperation with the obstetrician of a prominent American clinic. The first few chapters of this book are devoted to a discussion of the physiology of the heart and circulation in their relation to menstruation, pregnancy and labor. The various cardiac complications are thoroughly discussed. The management of a patient with heart disease in pregnancy and labor is considered. One can take little exception to these general considerations. Some of the rare conditions, such as congenital heart disease and bacterial endocarditis, are accorded more space than their rare occurrence deserves, but there is so little information concerning these conditions in textbooks and periodicals that these thorough discussions are highly desirable. In the author's discussion of the interruption of pregnancy for cardiac disease, he says that "it should now rarely be performed, for either a woman should not undertake pregnancy or she should be capable of carrying it through." This summarizes the value of preconceptional examination for the prospective mother. The volume represents a diligent survey of more than 1,000 references. A great amount of statistical data is thoroughly analyzed. These, plus the experiences of the author, provide an excellent outline of the heart in pregnancy. The work is a real contribution and can be heartily recommended to the obstetrician and the student of the problems of human reproduction.

Digrafía: Nuevo método radiográfico para el estudio de los órganos móviles. Por Guido Pollitzer. Paper. Pp. 104, with 41 illustrations. Buenos Aires: Imprenta amorrortu, 1937.

The author recognizes that probably the best method generally available for the study of the movement of organs is fluoroscopy, but even the most carefully made notes and the most tenacious visual memory will not permit comparisons of observations at different times. Stereoscopy does not serve the purpose. Radiocinematography is too expensive, both for the initial outlay for apparatus and for maintenance. Radiokymography has its disadvantages and is more expensive than the simple apparatus required for the author's method. A roentgenkymogram is a roentgenogram of an organ in movement obtained during a prolonged exposure. The "digram" (the author's term) is the production of instantaneous roentgenograms of an organ "surprised" in different positions. The roentgenkymogram registers all the movement, while the "digram" registers only the predetermined positions. The roentgenkymogram in spite of all these considerations gives a blurred image except on its borders, while the "digram" gives a clear image. The roentgenkymogram permits observations of only a small part of the detail of the image of the organ. The "digram" shows 50 per cent or at least one third of the organ. The "digram" is obtained by a frame superimposed on a cassette. In the frame is a grid having bars 3 mm. wide, separated by spaces exactly 3 mm. wide. Thus half the film is exposed when the grid is in one position. The grid is then changed and the half previously exposed is now covered and the other half now uncovered is exposed. A special viewing box permits one to see alternately the first and the second exposures at a slow or rapid rate, as may be desired. This method of viewing gives the illusion of a cinematographic record of movement. As a matter of fact, it is comparable to the commonly seen advertising signs where by a series of parallel shutters one may see first one sign and then another as the turning of the multiple parallel shutters alternately shows the one or the other. The "digraph" does not compete at all with the roentgenkymograph. It serves another purpose. The roentgenkymograph has had its chief value in recording the amplitude of the movements of the heart and in similar somewhat related studies, whereas the "digraph" will have considerable usefulness in recording and graphically reproducing such lesions as pleuropericardial adhesions, adhesions of the diaphragm, chest or the mediastinum, such as accompany nonopaque foreign bodies in the bronchus. The apparatus is not yet made in the United States but it should not be very expensive.

Chronic Intestinal Toxemia and Its Treatment with Special Reference to Colonic Therapy. By James W. Wiltsie, A.B., M.D., Consultant in Physical Therapy at the Binghamton City Hospital, Binghamton, N. Y. Cloth. Price, $3. Pp. 268, with 8 illustrations. Baltimore: William Wood & Company, 1938.

This is an earnest plea for the greater use of colonic irrigations. It is written by a physician who evidently is intelligent, earnest and thoroughly convinced of the value of the method. He starts out with somewhat of an inferiority complex, realizing fully that the medical profession has little faith in his hobby. It has no faith because it has been trying the method at intervals ever since the pyramids were built, and after each flare-up of favor it has watched the idea of intestinal intoxication die down again.

Today the principal users of the method are laymen, cultists and out-and-out charlatans. Obviously, any physician who hopes to overcome this handicap and convince the profession that it should again start washing colons must bring forward a large mass of well documented information. He must show that he is well educated, logical and thoroughly scientific in his presentation and weighing of evidence. His published case reports must show much clinical good sense, and perhaps most important of all, if he is going to convince unbelievers, he must face squarely and explain away all the evidence which they might bring against him. Side-stepping and sneering will not help.

Although this is probably the best written argument for the theory of chronic intestinal toxemia that has yet appeared, it still falls far short of being convincing and satisfying. Although there is much that seems scientific and clinically sound, there is also much that seems like pseudoscience.

One of the most curious features of the book is the author's insistence that the benefits of colonic lavage do not result from the emptying of the bowel but from some remarkable effect in "promoting tubular and cellular drainage, the healing of diseased tissues, the restoration of normal colon function, the improvement of both capillary and lymphatic circulation, and of liver function. The principle back of free drainage is that infection tends to disappear when drainage is adequate, and in the absence of a feeder."

It is startling also to find the use of enemas strongly deprecated as a most pernicious habit which under no circumstances should be started. According to Wiltsie the use of enemas by the patient himself actually tends to undo all the beneficial work that is accomplished by the colon washer in his office. Under such circumstances one should expect to find an exact and detailed explanation of the differences between an enema and an irrigation, but this we have not been able to find in the book.

One thing that will tend much to discourage the scientifically trained physician is the refusal of the author to face the large array of facts which are not favorable to his theory. These are hardly mentioned and, like most enthusiasts, the writer is inclined to quote only that scripture which is to his purpose. The well known fact that in many cases the symptoms of supposed autointoxication are produced reflexly by a distention of the rectum (as shown by the fact that relief comes immediately after defecation) is dismissed rather contemptuously.

It appears then that, although the book will be an excellent text for those who believe in colonic irrigations, it is not sufficiently convincing to induce a trained clinician or gastroenterologist to put a special table into his office and to start off trying to cure all sorts of diseases with this method.

Incidentally, one of the worst defects of the book is that the reader is left with doubts as to what are the indications for the use of this method. At least we are left with the idea that the essential point is to treat the patient with colonic washings, and then if he gets better, one can conclude that he was suffer-

ing from colonic toxemia. The physician who is at all philosophical and logical in his thinking always distrusts this type of argument, if only because with it one can go far to prove that faith healing and spine cracking are excellent modes of healing.

Die natürliche Heilweise im Rahmen der Gesamtmedizin. Eine Vortragsreihe, veranstaltet von der Berliner Akademie für ärztliche Fortbildung, Berlin NW 7, Robert-Koch-Platz 7. Herausgegeben von Professor Dr. Curt Adam, Leiter der Berliner Akademie für ärztliche Fortbildung. Paper. Price, 14 marks. Pp. 354, with 43 illustrations. Jena: Gustav Fischer, 1938.

This collection of postgraduate lectures for physicians is symptomatic of modern Germany. Its avowed purpose is that underlying the "new German healing art": the aim to secure a synthesis of scientific medicine with "folk medicine," even though scientific medicine is, after all, the daughter of "folk medicine." It has happened here, as it does in families, that the daughter has lost the appreciation of the wisdom of the mother, while the latter does not understand her daughter any more. It is the sick who suffer therefor, especially those patients for whom the "nature remedies" are prescribed. There is nothing radically different, however, in this series of addresses by various lecturers from the trends of pre-Nazi Germany in the extolling of the value of physical and dietetic remedies: an emphasis that, in this country, which has a tendency to neglect these therapeutic measures, is even more needed than it is in Germany. Unfortunately, the "synthesis" to be effected is with "homeopathy" and most especially "nature cure" empiricism without subjecting these to the strictures of scientific weighing and measuring and to emphasize the "immeasurable" as justification for doing this.

Injection Treatment of Varicose Veins and Hemorrhoids. By H. O. McPheeters, M.D., F.A.C.S., Attending Physician, New Asbury, Fairview and Northwestern Hospitals, Minneapolis, Minn., and James Kerr Anderson, M.D., F.A.C.S., Instructor in Surgery, University of Minnesota School of Medicine, Minneapolis. Cloth. Price, $4.50. Pp. 315, with 82 illustrations. Philadelphia: F. A. Davis Company, 1938.

This well written compact volume represents an authoritative and practical treatise. It is remarkably complete and yet brief enough to appeal to the busy practitioner. The chapters on anatomy and embryology as well as the other sections on the theoretical considerations of these subjects are excellent. The treatment of varicose veins and the complicating varicose ulcers is described in clear language based on the actual large experience of the authors. All the latest developments are considered and explained in simple language. Considering the voluminous literature that has appeared in recent years and the many controversial points in theory and technic that have been advanced, it is a relief to read a clear exposition which makes available a practical technic based on the best modern conceptions of these subjects. The section on the treatment of hemorrhoids by the injection method, which has been written by Dr. Anderson, is likewise noteworthy for its brevity and condensation into a practical monograph of the voluminous literature on this small but important subject to the general practitioner. The volume represents a type of medical textbook which is too infrequently published, a compact yet detailed practical handbook written in simple direct language containing the best of the latest in the treatment of varicose veins and hemorrhoids.

Neue biometrische Untersuchungen von Spermien und Fertilität. Von Dr. med. et phil. Konstantin D. J. Generales, jun. Paper. Price, 7 marks. Pp. 84, with 17 illustrations. Stuttgart: Ferdinand Enke, 1938.

It is now well recognized that in the clinical study of sterility in mated pairs of human beings a thorough examination of the male partner's semen is obligatory, and particularly a study of the morphologic and physiologic characteristics of the spermatozoa. There is also a growing recognition of the fact that detailed investigation of the individual germ cells may possibly be illuminating in cases of genetically grounded diseases and defects. This book is a useful contribution to the methodology of this field of inquiry. In addition to detailed instructions regarding the fixing, staining and measuring of sperm samples, elementary biometric technics are explained and exemplified. The author's own studies of individual variation in spermatozoa embodied in this book are based on the examination of more than 20,000 sperms. As strictly biometric indexes of quality (in the sense of fertilizing power) of spermatozoa, chief dependence is placed on (*a*) the product of the coefficients of variation for length and breadth of the sperm head, (*b*) the coefficient of variation for the volume of the sperm head, which however is not directly measured but is a derivative function of head length and breadth, and (*c*) the relation between the coefficients of variation for sperm head length and breadth in respect of their absolute magnitudes (fertilizing power being alleged to be diminished when $C_b - C_l > 1$). We incline to the view that most critical biometricians would be less trustful of the diagnostic indications derived from coefficients of variation than the author is. The mathematical structure of that constant has made most workers wary about putting too heavy a burden of interpretation on it. The book is clearly written and, even though probably not the final and definitive word on the subject, will certainly help toward its further scientific development.

A Text-Book of X-Ray Diagnosis. By British Authors. Edited by S. Cochrane Shanks, M.D., Physician, with Charge of Out-Patients, Departments of Radiology and Electro-Therapy, Charing Cross Hospital, London, Peter Kerley, M.D., M.R.C.P., D.M.R.E., Physician to the X-Ray Department, Westminster Hospital, London, and E. W. Twining, M.R.C.S., L.R.C.P., D.M.R.E., Radiologist, Royal Infirmary, Manchester. In three volumes. Volumes I and II. Cloth. Price, 50s; 42s. Pp. 591, with 398 illustrations; 458, with 307 illustrations. London: H. K. Lewis & Co., Ltd., 1938.

A comprehensive survey of the field of x-ray diagnosis sufficiently detailed for reference purposes and with an adequate bibliography has not been available heretofore in one publication in the English language. This work, projected in three volumes by a group of authoritative English radiologists and clinicians, attempts to fulfil this need. Although it does not measure up in all respects to its foreign language counterparts, the general plan is admirable. In each section are brief discussions of the normal anatomy, the pathology and the chief clinical features of the disease under consideration. This is followed by the roentgenologic features of the condition, occasional discussions of differential diagnosis and a reasonably adequate bibliography. X-ray technic is discussed only as it relates to strictly medical procedures. There is no general introduction to the subject of x-ray diagnosis, no effort at exposition of broad principles nor any other correlative material. The first volume contains a section on the cardiovascular system by Kerley which is only fairly well done. All the information is sound and it is easily read. The illustrations are too few and the subject is insufficiently detailed. X-ray examination of the peripheral vessels is also covered in this section. The second section, on the respiratory tract, by Twining, is excellent. The discussion of fluoroscopic technic and general principles underlying the examination of the lungs is particularly good. The author describes in some detail his simple method of tomography and its application to pulmonary diagnosis. The final section, on the urogenital tract, by Marshall and Shanks, is well presented.

The second volume contains a section on the alimentary canal by Shanks. Gastric ulcer and postoperative gastric conditions are both splendidly detailed. In other respects, however, this section is disappointing. There is little attention to differential diagnosis and the illustrations are clearly insufficient. No reproductions of esophageal varices, gastrojejunocolic fistula or bezoars of the stomach, to mention a few, are given. The section on the biliary tract, by Kerley, is well written with a sufficiency of detail. His account of the appearances in biliary dyskinesia is of particular interest. There is, in addition, in this volume a fairly good discussion of the abdomen, in general, by Shanks and an excellent section on the roentgenologic aspects of obstetrics and gynecology by Roberts and Wilson. The third volume, on the bones and joints and the nervous system, has not yet been published.

There is throughout a regrettable absence of any reference to accuracy or dependability of the x-ray examination. For example, in the detailed and otherwise satisfactory discussion of miliary tuberculosis there is no mention of the fact that weeks may occasionally pass before the roentgenologic aspects of this condition become apparent. It is strange to find so little reference to pneumoperitoneum, which is covered only in relation to gynecology. In the discussion on intestinal obstruction, an extremely important indication for roentgenographic study, the information is most inadequate. There is no reference whatever to retroperitoneal or paraduodenal hernia. American roentgenologists will certainly not agree that filling of the terminal

ileum during examination of the colon is an "undesirable accident." Aside from this, however, there are few statements to which exception can be taken. The bibliography is fairly good but is somewhat marred by glaring typographical errors, such as Schwick for Swick, Davies for Davis, and Chester for Stewart. It is almost incredible that the bibliography of a section on the stomach and duodenum should have omitted all reference to the work of Lewis Gregory Cole. The illustrations, less than 400 for each volume, are too few for a reference book. They are, with few exceptions, reproduced as positives. The printing and figuring are of satisfactory quality. The too few diagrams and elaborately labeled illustrations are excellent.

Despite many deficiencies, these volumes represent an important effort to correct a serious deficiency in our literature. The whole work will no doubt form an indispensable part of every roentgenologist's library and will prove of great value to all who need authoritative reference to the details of x-ray diagnosis.

The Single Woman and Her Emotional Problems. By Laura Hutton, B.A., M.R.C.S., L.R.C.P. With a foreword by David Forsyth, M.D., F.R.C.P. Second edition. Cloth. Price, $1.50. Pp. 173. Baltimore: William Wood & Company, 1937.

This small volume, by an English woman physician, is written for laymen, more particularly for single women. It is a book, however, that can be read with profit by most physicians as well. The author briefly reviews the position of the single woman today. The problem of the single woman has become a more pressing one in countries involved in the World War, since the potential mates of many thousands of women were killed. The modern psychology, emanating chiefly from Sigmund Freud, that offers the basis on which the author discusses her thesis is skilfully if necessarily incompletely outlined. The psychologic problems of friendships among women, sexual problems and sexual inversion are dealt with. Dr. Hutton approaches her thesis not from the standpoint of psychopathology but rather as the problems ordinary women subjected to the special tensions and difficulties associated with a lonely or at least a manless existence are faced with. Her treatment of these problems is sympathetic, humane and scientifically sound. The book can well be read by most intelligent women who face the prospect of a life without marriage.

Studien über die Entstehung und Entwicklung der Lungentuberkulose mit besonderer Berücksichtigung des Verlaufs der tuberkulösen Erstinfektion des Jugendlichen und Erwachsenen. Von Haqvin Malmros und Erik Hedvall. Unter Mitwirkung der Röntgendiagnostischen Abteilung (Chefarzt: Dozent H. Hellmer) des Universitätskrankenhauses zu Lund. Nr. 68, Tuberkulose-Bibliothek, Beihefte zur Zeitschrift für Tuberkulose. Herausgegeben von Dr. Franz Redeker, Oberregierungs- u. Obermedizinalrat, Berlin, und Dr. Karl Diehl, dirigierender Arzt, Sommerfeld. Paper. Price, 27 marks. Pp. 223, with 140 illustrations. Leipzig: Johann Ambrosius Barth, 1938.

Periodic study with tuberculin test and x-ray examination of more than 3,000 young men and women at the University of Lund in southern Sweden permitted the authors to observe the development of pulmonary lesions in 133 students. Their observations dealing with the genesis of tuberculosis are of great importance. The studies were carried out with thoroughness and the results are reported in detail. Only rarely was the "subclavicular infiltrate" found to be the earliest lesion. As a rule the initial manifestation of pulmonary tuberculosis was above the clavicle, indicated by discrete soft spots in the x-ray film. Spread below the clavicle was usually followed by confluence of the spots, simulating a primary exudative infiltrate. Apical infiltrations of this sort were frequently noted, without evidence of a primary complex, in students who had only recently become tuberculin positive. Apical lesions progressed to clinical disease and occasionally to death, with equal frequency in students recently infected and in those long positive to tuberculin. The authors warn that apical or subapical lesions must be considered serious even when they are believed to be of first infection type. Illustrative roentgenograms, reproduced with remarkable clarity, greatly enhance the value of this report. The progression of tuberculosis from minute apical infiltrations to advanced disease can be plainly followed in these excellent reproductions. This volume will prove of exceptional value to physicians interested in the pathogenesis of tuberculosis and will be highly useful to roentgenologists, who will find it a comprehensive atlas of the early lesions of pulmonary tuberculosis.

Practical Otology. By Morris Levine, M.D., F.I.C.S., Clinical Professor of Otolaryngology, New York Post-Graduate Medical School, Columbia University, New York. Second edition. Cloth. Price, $5.50. Pp. 416, with 149 illustrations. Philadelphia: Lea & Febiger, 1938.

This popular small book on diseases of the ear consists essentially of a compilation of lectures given by the author for the New York Post-Graduate Medical School of Columbia University. The book is short and concise, written in an easily readable style. There is not much detail or theory, which the author defends in his preface for reasons which appear good to him. Hence, though it is an excellent book for medical students, general practitioners and perhaps those starting the practice of otology, it is not complete enough for the practicing specialist. The descriptions of disease are good. The chapters on acute otitis media and mastoiditis are among the best in the book and are worthy of praise. There is an excellent chapter on petrositis which summarizes most of the new thought on this subject. If there is any criticism of the book it lies in the preliminary chapters. In spite of the fact that the author prefers not to consume too much space in the discussion of theories and debatable points, it does not seem altogether fitting that a book published in 1938 should omit those newer studies of otology pioneered by Wever, Bray and others, and which have given such impetus to theory and practice in recent years.

Comparative Study of the Marmas. By P. V. Krishna Rao, B.A., M.B., B.S., Professor of Physiology and Hygiene, Govt. Indian Medical School, Madras. Cloth. Price, 5s. Pp. 68, with illustrations. Madras: P. Varadachary & Co., 1937.

The word Marma is derived from the Sanskrit root "Mru," "Marane" and it applies to a place of vital importance in the body which, if injured, results in serious consequences or death sooner or later. Surgeons of ancient India laid down the rule that in a case of surgical operation the situation and the dimension of each local marma should first be studied well and the incision for operation made in such a way as to avoid even the edge of a marma. The knowledge of the marmas was made use of in ancient warfare and in hunting after wild animals by aiming at the marmas with the arrows. This science is also practiced in the art of wrestling in some parts of India and Japan. The author has extracted the relevant passages from Hindu Scriptures and translated them into English. He describes, in the light of modern anatomy, the structure of each "marma" with its corresponding anatomic parts, with their names according to the western system. The author then prescribes medicines and methods of treatment for disorders of each affected "marma." These are derived from his own private practice and not from any standard Hindu works. It is doubtful whether modern medicine would approve this part of the book. The "marmas" themselves are still authentic.

Personal Hygiene. Compiled by Robert Olesen, Assistant Surgeon General, United States Public Health Service. Supplement No. 137 to the Public Health Reports. U. S. Treasury Department, Public Health Service. Paper. Price, 10 cents. Pp. 46, with illustrations. Washington, D. C.: Supt. of Doc., Government Printing Office, 1938.

Health maintenance is largely a personal responsibility. This short compilation of information concerning personal hygiene, originally prepared for radio use, has been revised and brought down to date. Cleanliness, immunization against infectious diseases, school hygiene, food, posture, sport, care of the hair and scalp, and first aid are among the subjects briefly but clearly discussed. A short bibliography is appended. This booklet serves as a useful guide to a few of the phases of personal hygiene.

A Manual of Tuberculosis for Nurses and Public Health Workers. By E. Ashworth Underwood, M.A., B.Sc., M.D., Medical Officer of Health, County Borough of West Ham. With an introduction by Professor J. R. Currie, M.A., M.D., F.R.C.P., Professor of Public Health in the University of Glasgow. Second edition. Cloth. Price, $3.25. Pp. 404, with 53 illustrations. Baltimore: William Wood & Company, 1938.

For nurses on duty with tuberculous patients this book is excellent. The manner of infection and description of primary and secondary types are well handled. The description of symptoms, what produces them and what a nurse might do is carefully explained. Sanatorium care, together with an explanation of what is to be expected from such treatment, is given in detail. All a nurse should know about the surgery of all forms

of tuberculosis is set forth. From the point of view of the public health worker and preventive medicine the book is not all inclusive. This phase of tuberculosis is not presented in sufficient detail. Had the title omitted "public health workers" the work would accomplish its purpose.

Berättelse från styrelsen för cancerföreningen i Stockholm över verksamhetsåret 1937. Index of Papers Published at Radiumhemmet 1909-1937. Report on Cases Treated at Radiumhemmet 1921-1937. Paper. Pp. 103. Stockholm: K. L. Beckmans Boktryckeri, 1938.

The list of papers contains 287 titles. The tabular summary of the results of treatment covers 55,038 cases grouped under 879 different disease conditions. Any details of treatment are not given.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Workmen's Compensation Acts: Recovery Retarded by Mental Sequelae of Industrial Injury.—Vallee had a spinal malformation and chronic bronchitis. In the course of his employment, April 3, 1936, four of his ribs were fractured, one rib piercing a lung. His employer paid him full compensation from April 3 to Oct. 12, 1936, and thereafter refused to pay him anything. In a proceeding instituted under the workmen's compensation act, the trial court awarded the workman compensation on the basis of total disability to April 3, 1938, and of partial disability from then to April 3, 1940. The employer thereupon brought exceptions to the Supreme Court of New Hampshire.

The employer's argument, said the court, is substantially fallacious in its insistence that the direct consequences of the accident are limited to the immediate consequences. Any aggravation of the claimant's spinal malformation or of the bronchitis, by the accident or the consequences thereof, was properly attributed to the accident. Furthermore, the mind, as well as the body, may be hurt by a traumatic injury. If conditions arising in the course of recovery affect the mind in such a way as to retard convalescence, the resulting prolongation of disability may be attributed to the accident. Loss of work and of bodily strength and activity may cause depression or melancholy which, even though mild, may prolong disability.

The defendant's medical expert testified that the plaintiff's condition was partly due to his injury, that some soreness from the broken ribs persisted and greatly worried him, and that he was suffering from "a mental condition to a large extent which started at the time of the accident." This mental condition, the witness testified, accounted for the workman's feelings of weakness and loss of strength whenever he tried to do any work. He further testified that the workman's complaints of backache were due to the long time he had been out of work, his apprehensions about himself, the long period of sitting around and disuse of his back muscles, so that they had become soft and weak. This evidence, the court said, together with that tending to show that before the accident the workman worked steadily while thereafter he was unable to work except to a negligible extent, that his general health was poor after the accident, that he lost 15 pounds in weight and became anemic, that he had severe back pains and that his complaints were not of pretended suffering, was sufficient to support the findings of the trial court. Although the workman's back was not hurt in the accident, the court thought it reasonable to infer that inactivity due to the accident brought about some condition in connection with his spinal deformity which caused suffering from it, and although his chronic bronchitis was progressive as time went on, it was a fair deduction that the accident developed and increased the speed of its progress.

After reviewing carefully the entire record, the Supreme Court was of the opinion that the award of compensation made by the trial court to the workman was justified.—*Vallee v. Spaulding Fibre Co. (N. H.), 197 A. 697.*

Optometry Practice Acts: Revocation of Optometrist's License Because of Corporate Employer's Use of Prohibited Advertising.—The Minnesota optometry practice act authorizes the state board of optometry, after notice and hearing, to revoke the license of any licentiate found guilty of conduct of a character likely to deceive or defraud the public, including such practices as price advertising, advertising free examinations, splitting fees or the use of untruthful, improbable, misleading or impossible statements in connection with practice or treatment. The act authorizes the board to make any rules and regulations, not inconsistent with law, which it may deem necessary for the effective enforcement of the act. The board undertook, by rule 6, to declare that unprofessional conduct would be imputed to a licensed optometrist employed by a firm or corporation if his employer engaged in any advertising prohibited by law or board rule. The plaintiff, a licensed optometrist, was charged, in a revocation proceedings, with being in the employ of a jewelry company that used types of prohibited advertising, that he, the plaintiff, aided and abetted his employer in doing so, and that he was therefore guilty of unprofessional conduct. The district court, Ramsey County, at the instance of the plaintiff, enjoined the board from revoking the plaintiff's license, and the board appealed to the Supreme Court of Minnesota.

In the opinion of the Supreme Court, the board was without power to revoke the plaintiff's license under the circumstances stated. Since the optometry practice act, said the court, provides that unlicensed persons may sell optometric articles if such sale is under the control and direction of a licensed optometrist who is in charge of and in personal attendance at the place where such articles are sold, clearly it is lawful for a licensed optometrist to accept such employment. The employment being lawful, it seemed to the court to be contrary to the letter and spirit of the law to hold the employee responsible for the employer's violation of the law and to impute knowledge of such violations to the employee. If the employer violates the act in any manner, he may be enjoined or prosecuted. There is no right or justice in punishing the servant for the misdeeds of the master. The court did not overlook the fact that the complaint filed with the board charged that the plaintiff aided and abetted his employer, but the court thought that it was clearly evident from a reading of the complaint as a whole that that allegation was a conclusion drawn from the fact that the plaintiff did not quit the employment when informed of the employer's transgressions.

The primary purpose of optometry legislation, continued the court, is the protection of human eyesight. Such legislation was not enacted to further the personal interests of the optometrists except so far as their advancement in skill and efficiency serves the primary purpose of the law. When the purchaser of eyeglasses has the services of a competent licensed optometrist in selecting and fitting them to his eyes, he has had all the benefits the law intended.

The Supreme Court accordingly affirmed the judgment of the trial court enjoining the board from revoking the plaintiff's license.—*Williams v. Mack (Minn.), 278 N. W. 585.*

Society Proceedings

COMING MEETINGS

American Academy of Orthopedic Surgeons, Memphis, Tenn., Jan. 15-19. Dr. Carl E. Badgley, 1313 East Ann St., Ann Arbor, Mich., Secretary.

American Association for the Study of Neoplastic Diseases, Baltimore, Dec. 28-30. Dr. Eugene R. Whitmore, 2139 Wyoming Avenue N.W., Washington, D. C., Secretary.

American Student Health Association, New York, Dec. 29-30. Dr. Ruth E. Boynton, Students Health Service, University of Minnesota, Minneapolis, Secretary.

Eastern Section, American Laryngological, Rhinological and Otological Society, Boston, Jan. 11. Dr. Frank E. Kittredge, Masonic Temple, Nashua, N. H., Chairman.

Middle Section, American Laryngological, Rhinological and Otological Society, Sioux City, Iowa, Jan. 19-20. T. R. Gittins, Davidson Bldg., Sioux City, Iowa, Chairman.

Southern Section, American Laryngological, Rhinological and Otological Society, New Orleans, Jan. 14. Dr. Francis E. LeJeune, Maison Blanche, New Orleans, Chairman.

Western Section, American Laryngological, Rhinological and Otological Society, Spokane, Wash., Jan. 29. Dr. Frederic G. Sprowl, Medical Arts Bldg., Spokane, Wash., Chairman.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1928 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Medical Jurisprudence, Boston

1: 73-144 (Oct.) 1938

Legal Phases of Psychiatry. A. Myerson, Boston.—p. 73.
Accidents in Radiology. E. H. Skinner, Kansas City, Mo.—p. 79.
Validity of Postmortem Tests for Alcoholism. R. E. Cornish, H. D. Draper and J. Finn Jr., Berkeley, Calif.—p. 86.
Carbon Monoxide Poisoning. W. D. McNally, Chicago.—p. 89.
The Work of a Medical Examiner's Office: Description of How It Is Accomplished in New York City. B. M. Vance, New York.—p. 95.
Preliminary Survey of 1,000 Case Histories of Inmates of the Elmira Reformatory. R. Breguet, Elmira, N. Y.—p. 101.
Medical Testimony. H. E. Mock, Chicago.—p. 119.

Annals of Surgery, Philadelphia

108: 801-960 (Nov.) 1938

Observations on Mode of Action of Sulfanilamide and Its Application to Surgical Infections. J. S. Lockwood, Philadelphia.—p. 801.
Toxic Manifestation of Sulfanilamide. P. H. Long and Eleanor A. Bliss, Baltimore.—p. 808.
Effect of Sulfanilamide on Human, Virulent Hemolytic Streptococci. C. Lyons, with technical assistance of Anita Mangiaracine, Boston.—p. 813.
Treatment of Hematogenous Nephritis with Sulfanilamide: Case Report. H. H. Young and S. A. Vest, Baltimore.—p. 828.
Treatment of Intraperitoneal Abscess Arising from Appendicitis. E. P. Lehman and W. H. Parker, University, Va.—p. 833.
Regional Enteritis. C. F. Dixon, Rochester, Minn.—p. 857.
Perianal Fistulas as Complication of Regional Ileitis. A. Penner and B. B. Crohn, New York.—p. 867.
*Acute Cholecystitis: Results of Operation Within Forty-Eight Hours of Onset of Symptoms. H. F. Graham and M. E. Hoefle, Brooklyn.—p. 874.
Epidermoid Cysts of the Spleen. A. H. Montgomery, E. T. McEnery, Chicago, and A. A. Frank, Malden, Mass.—p. 877.
Embryoma of Kidney (Wilms' Tumor). W. E. Ladd, Boston.—p. 885.
Therapeutic Management of Urinary Infections. A. Randall and B. Hughes, Philadelphia.—p. 903.
*Thymol Therapy in Actinomycosis. T. M. Joyce, Portland, Ore.—p. 910.
*The Problem of Wound Healing: Effect of Local Antiseptic Agents on Infected Wounds. D. P. Anderson Jr., Philadelphia.—p. 918.
Effect of Urinary Bladder Transplants and Extracts on Formation of Bone: Further Experimental Study. G. H. Copher, St. Louis.—p. 934.
Apparent Alteration of Tetanus Toxin Within Spinal Cord of Dogs. W. M. Firor and A. Lamont, Baltimore.—p. 941.

Acute Cholecystitis.—Of 167 patients with acute cholecystitis on whom Graham and Hoefle operated within forty-eight hours of the onset, death occurred in six. Cholecystectomy was the operation of choice in these cases, while cholecystostomy was reserved for the more critical ones. Certain factors make a cholecystectomy for acute cholecystitis more difficult than one performed in the quiescent period. The gallbladder is often tense and distended. The tissues are more friable and the bleeding is more profuse. There is more swelling around the cystic duct. It may be necessary to aspirate the gallbladder, and the authors usually prefer in these acute cases to remove it from above downward, controlling the bleeding from the liver bed by the pressure of a gauze pad and a retractor. An oozing liver bed that cannot be obliterated can be quickly peritonealized and rendered dry by a free omental graft lightly tacked in place by a few interrupted sutures. A large percentage of cultures taken during the first forty-eight hours remain sterile and therefore infection is not a major problem at this time. Acute cholecystitis is not like acute appendicitis and there is not the same necessity for prompt operative intervention. But of twenty-seven patients operated on within two to five days of onset two died and of twenty-two operated on five or more days after onset five died. It is seen that a delay of more than five days gives a high operative mortality and raises the question of whether operation should be performed or further delay advised. This must be decided for each individual case. A lowering in mortality can be accomplished by education of the public and cooperation between the family physician and the surgeon to secure a prompt operation, early in the attack, for every person suffering from acute cholecystitis who is a good operative risk.

Thymol Therapy in Actinomycosis.—Joyce believes that the most effective treatment of actinomycosis is a combination of radical surgical intervention and thymol medication. His procedure is to give orally 1.5 Gm. of powdered thymol in capsules two out of every three days, to open the sinuses widely, to curet and fill them with thymol in olive oil (10 per cent solution) and then to inject the sinuses each day. Small strips of gauze are inserted to keep the sinuses open.

Wound Healing.—In an attempt to ascertain the exact value of topical agents in the treatment of infected wounds, Anderson measured precisely the changes in the size and bacterial count of twenty wounds. The wounds studied differed in size, etiology and bacterial flora, but each was of the type regarded as surgically infected. The majority of infected wounds, adequately drained and not containing sloughing tissue, in normal persons will heal according to a regular geometric curve, the rate being proportional to the size of the wound and decreasing with the age of the patient, regardless of the type of local treatment. Invasive organisms, extensive necrosis and the presence of dead tissue in the wound, even without active infection, retarded healing. The presence of a large number of organisms on the surface of wounds does not ordinarily retard healing. Local agents considered had little or no beneficial effect on the healing of infected wounds, except for the action of zinc peroxide in specific cases. The few antiseptic agents which had definite bactericidal action on surface organisms in normal granulating wounds were ineffective in the presence of tissue necrosis, and it is only under the latter circumstances that the existing infection is likely to retard healing. In the management of infected wounds, less attention should be given to the selection of a potent local antiseptic agent. It is of more importance to consider the problem of increasing local tissue immunity, which may be influenced by factors of a general nature remote from the site of the wound, and aiding the sequestration of necrotic tissues rich in bacteria by mechanical or chemical débridement and adequate surgical drainage.

Archives of Ophthalmology, Chicago

20: 709-906 (Nov.) 1938

Implantation of Hollow Grooved Body into Orbit for Filling Late After Enucleation of Eyeball. J. M. Wheeler, New York.—p. 709.
Determination and Significance of Scotopic Retinal Visibility Curve. E. Ludvigh, Boston.—p. 713.
Physiologic and Clinical Ophthalmologic Problems in Relation to Individual Variability. A. Brückner, Basel, Switzerland.—p. 726.
Congenital Buphthalmos Complicated by Dislocation of Lens and Hemorrhage into Vitreous with Complete Recovery of Central Vision. W. J. Holmes, Warren, Ohio.—p. 757.
Circulation of Aqueous: VII. Mechanism of Secretion of Intra-Ocular Fluid. J. S. Friedenwald and R. D. Stiehler, Baltimore.—p. 761.
Coloboma of Optic Nerve and of Macula: Microscopic Study. D. Wexler and M. Last, New York.—p. 787.
Acute Alcoholic Amaurosis. F. D. Carroll and R. Goodhart, New York.—p. 797.
*Panophthalmitis and Sympathetic Ophthalmia. B. Samuels, New York.—p. 804.
Experimental Hypertension: VIII. Vascular Changes in the Eyes. J. E. L. Keyes and H. Goldblatt, Cleveland.—p. 812.
Reading Difficulties in Children. G. E. Berner and Dorothy E. Berner, Philadelphia.—p. 829.
Carbon Disulfide Poisoning. R. McDonald, Philadelphia.—p. 839.

Panophthalmitis and Sympathetic Ophthalmia.—Samuels points out that panophthalmitis is of relatively rare occurrence today, not only because severely injured eyes are excised before the infection is far advanced but because the usual infecting germs do not lead to a widespread purulence. However, in regions with warm climates it is still relatively frequent, whereas in the United States it probably represents not more than 2 or 3 per cent of all intra-ocular infections following injuries. Of 101 globes showing characteristic sympathetic tissue, reported in a previous paper, there were only three which had been affected with panophthalmitis. In this same series there were nine instances of typical sympathetic infiltration of the choroid without involvement of the fellow eye. Of these nine, seven followed common endophthalmitis and two followed panophthal-

mitis. Thus three cases of panophthalmitis in a series of 101 cases of sympathetic ophthalmia is not an insignificant figure and suggests that a panophthalmitic eye may not be so harmless as has been commonly thought.

Archives of Surgery, Chicago

37: 697-864 (Nov.) 1938

Ovarian Dysgerminoma. G. E. Seegar, Baltimore.—p. 697.
*Infections of the Hand: Three Years' Experience in a Clinic for Study of Whitlow. E. A. Devenish, London, England.—p. 726.
Treatment of Intestinal Obstruction. J. Bottin, Liége, Belgium.—p. 735.
Spreading Peritonitis Complicating Acute Perforative Appendicitis: Experimental Studies. J. O. Bower, J. C. Burns and H. A. Mengle, Philadelphia.—p. 751.
Degeneration of Infundibular Nerve Fibers in the Cat Without Appreciable Polydipsia. A. D. Keller and J. W. Hamilton Jr., University, Ala.—p. 760.
*Serum Therapy for Infections with Streptococci: General Observations. Adele E. Sheplar, Martha Jane Spence and W. J. MacNeal, New York.—p. 772.
Hepatic Damage in Biliary Disease: Its Relation to Concentration of Bile Acids in the Bile. H. K. Gray, J. M. McGowan, W. S. Nettrour and J. L. Bollman, Rochester, Minn.—p. 790.
Technic of Ivory Implant for Correction of Saddle Nose. M. M. Wolfe, Philadelphia.—p. 800.
Duodenal Ruptures. A. Lurje, Ivanovo, U. S. S. R.—p. 808.
*Maggot Therapy for Hematogenous Osteomyelitis of the Tibia. S. Maddock, with the assistance of Dorothy Jensen, Boston.—p. 811.
End Results of Tuberculous Cystitis: Report of Cases. J. B. Wear, Madison, Wis.—p. 821.
Cysts of External Semilunar Cartilage: Report of Three Cases. S. Kleinberg, New York.—p. 827.
Review of Urologic Surgery. A. J. Scholl, Los Angeles; F. Hinman, San Francisco; A. von Lichtenberg, Budapest, Hungary; A. B. Hepler, Seattle; R. Gutierrez, New York; G. J. Thompson, J. T. Priestley, Rochester, Minn.; E. Wildbolz, Berne, Switzerland, and V. J. O'Conor, Chicago.—p. 835.

Infections of the Hand.—Devenish states that during a period of three years 388 patients with infections or injury of the hand were seen at the University College Hospital. There were sixty-one cases of injury, leaving 327 cases of infection (whitlow), in 192 of which there was a history of injury. Of the cases of infection of the digital pulp, of paronychia and of subcutaneous abscess and cellulitis of the fingers, trauma occurred in 64, 50 and 65 per cent, respectively. With the other types of whitlow the figures were not large enough to indicate the significance of trauma. If trivial injury received prompt treatment, the incidence of whitlow was much reduced. Such measures are immediate cleansing of the wound, its protection against contamination and a warning to the patient to report immediately if the lesion becomes painful. At present so much attention is focused on the site of the incision and the necessity for early operation "to relieve tension" that unnecessary operations are apt to be encouraged. Premature incision for spreading cellulitis is by no means a harmless blunder; it may determine the onset of sloughing. It is more difficult to abort an infection of the pulp than to arrest cellulitis elsewhere in the hand, but this is probably due to the situation of the pulp at the end of the arterial tree of the upper limb. Premature incision for cellulitis of the pulp is thus more likely to result in extensive sloughing and may possibly cause necrosis of the terminal phalanx. Swelling and congestion of the inflamed area are reduced to a minimum by elevation of the limb and immobilization. Splinting for immobilization or elevation must not interfere with the circulation. The hand seems to be dependent for efficiency on constant use. Complete disuse, whether produced by therapeutic immobilization or by a tender scar, is followed by atrophic changes in the fingers, which result in their disablement. This may be prevented in the former instance by discontinuing immobilization and by starting active movements as soon as healing is established.

Serum Therapy for Streptococcic Infections.—Sheplar and her associates report sixty-six severe cases of streptococcic infection, seen in consultation, treated with concentrated antistreptococcus serum. The youngest patient was 19 days old and the oldest 80 years. Of the sixty-six patients, eighteen died. There were six patients with diffuse bacterial meningitis and two with generalized peritonitis, types of disease in which the serum at present available does not offer much hope. In only three of the eighteen cases was the effect of the serum really disappointing. Five successful cases are cited illustrating the use of the serum under varied conditions. The first is an example of temporary invasion of the blood stream from lesions on the hands, treated by subcutaneous injections of concentrated state serum to a total amount of 40,000 units. The patient recovered promptly from the infection. The second patient was desperately ill with streptococcic pneumonia, empyema and bacteremia. She was treated with polyvalent streptococcus serum from February 10 to April 2 and the total amount of serum used was 760 cc.; this treatment was augmented by multiple transfusions and surgical drainage of the pleural cavity. The third patient, with postoperative streptococcic infection, was treated with the regular (unconcentrated) serum of the New York state department of health. The first administration of the serum (25,000 units) on May 16 was followed by improvement. An injection of 5,000 units of the serum was given on May 20. After a period of improvement there were a relapse and extension of the inflammation and on May 29 more serum was given in divided doses, to a total amount of 15,000 units. This was followed by 10,000 units on May 30 and 5,000 units on each of three consecutive days. This time there was prompt improvement without further relapse. The fourth patient had postoperative streptococcic infection. A streptococcus bacteriophage was applied to the wounds and 40,000 units of concentrated streptococcus serum (New York state) was given intramuscularly on each of two days. The last patient was treated with sulfanilamide in moderate doses for four days and with streptococcus serum on these four days and for eight days thereafter. She made a rapid recovery. There was no incompatibility between the serum and sulfanilamide or streptococcus bacteriophage employed simultaneously. There is reason to believe that superior results may be obtained by the careful use of these agents in combination. The authors propose to designate as the Hugh Young reaction the chill, sudden rise in temperature, diaphoresis and fall in temperature so often observed in the treatment of sepsis when an adequate amount of the antibacterial agent has been introduced into the blood stream to initiate the eradication of the infecting bacteria.

Maggot Therapy for Hematogenous Osteomyelitis.—Maddock used maggot therapy in the treatment of twenty-nine cases (thirty-one lesions) of hematogenous osteomyelitis of the tibia. Most of the patients had been operated on by other surgeons, and treatment with maggots was begun after a period of antecedent treatment. The great advantage in the use of maggots seems to lie in the high percentage of closed lesions and in the relative scarcity of recurrences. This is doubtless due to the ability of the larvae to uncover hidden sequestrums and to seek out small abscesses which might otherwise become included in the new bone. Maggot therapy is not indicated in all cases of osteomyelitis. Only when the patient fails to make reasonable progress clinically is it necessary to consider the use of maggots. For chronic osteomyelitis their usefulness is probably much greater. After seven years of experience and many trials of various substitutes the author still feels that the condition can be treated profitably with maggots and that no lesion should be given up as hopeless until maggot therapy has been tried. Of the thirty-one lesions, twenty-six up to the time of writing were closed, one still required treatment, two had necessitated amputation and two patients were lost track of.

Bulletin of Neurol. Inst. of New York, New York

7: 95-210 (Sept.) 1938. Partial Index

Relapsing Juvenile Chronic Subdural Hematoma: Clinical and Roentgenographic Study. L. M. Davidoff and C. G. Dyke, New York.—p. 95.
Comparison of Series of Olfactory and Visual Tests for Localization of Tumors of the Brain. C. A. Elsberg and H. Spotnitz, New York.—p. 165.
Subjective Foveal Hemianopsia During Dark Adaptation in Patients with Tumors of Temporal Lobe. H. Spotnitz, New York.—p. 170.
Myeloscopy: Diagnostic Inspection of Cauda Equina by Means of an Endoscope (Myeloscope). J. L. Pool, New York.—p. 178.
Comparison of Spinal Fluids in Active and Inactive Cases of Multiple Sclerosis. S. M. Dillenberg, New York.—p. 190.
Comparison of Symptoms of Glioblastoma Multiforme and Fibrillary Astrocytoma of Temporal Lobe. R. T. Collins, New York.—p. 195.
Laterality of Signs and Symptoms in Series of Pathologically Verified Tumors of the Brain. T. E. Bamford Jr., New York.—p. 201.

Canadian Medical Association Journal, Montreal

39: 419-516 (Nov.) 1938

Progress in Ophthalmology. S. Duke-Elder, London, England.—p. 419.
Rheumatic Fever. J. C. Meakins, Montreal.—p. 426.
Unusual Findings in Case of Acute Mercurial Poisoning. I. M. Rabinowitch, Montreal.—p. 429.
One Hundred Broken Noses. J. W. Gerrie, Montreal.—p. 433.
Tattooing of the Cornea. J. N. Roy, Montreal.—p. 436.
Congenital Hernia into Umbilical Cord: Two Cases, One Associated with Persistent Cloaca. C. W. Burns and M. A. Ogryzlo, Winnipeg, Man.—p. 438.
Calcium Carbonate Deposits in Human Gallbladder. A. T. Cameron, F. D. White and Sara Meltzer, Winnipeg, Man.—p. 441.
Experimental Production of Peptic Hemorrhagic Esophagitis. H. Selye, Montreal.—p. 447.
Risk of Spinal Puncture. H. H. Hepburn, Edmonton, Alta.—p. 449.
*Facial Paralysis Complicating Mastoid Operations. J. A. Sullivan, Toronto.—p. 451.
A Résumé on Undulant Fever: Use of Prontosil and Prontylin: Report of Two Cases. R. H. Fraser, F. D. White and M. B. Perrin, Winnipeg, Man., with collaboration of Esther B. Hardistry, Vancouver, B. C.—p. 455.
*Amyloidosis of Adrenals as Cause of Addison's Disease. D. L. Mendel and M. Saibil, Montreal.—p. 457.
*Significance of Low Leukocyte Count in Acute Pyogenic Infections. C. H. Watson and T. R. Sarjeant, Toronto.—p. 460.
What Report Should a Physician Expect from a Dentist? G. A. Morgan, Toronto.—p. 465.
Common Errors in Certifying Cause of Death on Medical Certificate. A. H. Sellers, Toronto.—p. 468.

Facial Paralysis Complicating Mastoid Operations.—Sullivan bases his conclusions on his reparative operative experiences in sixty cases of facial nerve palsies and anatomic dissections of the temporal bones of animals. 1. The systematic identification of the sigmoid sinus plate, the horizontal canal, the digastric crest, traced forward to the posterior bony canal wall, and the joining together of the latter two structures reveals a plane for the position of the vertical segment. 2. The tympanic segment of the nerve may be injured in the simple mastoid operation. The position of the horizontal canal is fixed, the anterior margin of which is the posterior border of the fallopian aqueduct. Therefore this structure must constantly be observed in opening the mastoid antrum, as in reality it affords a protection to the nerve. 3. In the radical operation the tympanic segment must be visualized. The "bridge," so called, should never be removed by any manipulation directed from the middle ear toward the mastoid antrum. 4. The nerve in sclerotic bone is more superficial on the tympanic aspect of the posterior bony canal wall, the so-called pyramidomastoid segment, and is most prone to injury in the lowering of the hypotympanum and the removal of the bony margin of the annulus tympanicus on this surface. 5. Handled thus, facial paralysis complicating the mastoid operation is on the way toward coming under surgical control, the prognosis, heretofore invariably grave, will give better promise and the malady will be less and less common.

Amyloidosis of Adrenals as Cause of Addison's Disease.—Mendel and Saibil present a case of Addison's disease developing on the basis of amyloidosis in the course of pulmonary tuberculosis, with no evidence of tuberculosis in the adrenals, an apparently uncommon occurrence. The adrenals are frequently involved in the course of generalized amyloidosis, yet Addison's disease on this basis is extremely rare. It appears to depend on the degree of amyloid infiltration and the extent of clinical development of the syndrome of Addison's disease.

Low Leukocyte Count in Pyogenic Infections.—After determining the leukocyte and polymorphonuclear counts in cases of appendicitis, pneumonia and other pyogenic infections, Watson and Sarjeant believe that the sequence of events in leukocytosis is as follows: 1. During the early stages of a severe pyogenic infection there is a rapid production of leukocytes, which are delivered to the blood as young forms. This causes an increase in the total leukocyte count and a shift to the left in the polymorphonuclear count. 2. The white cell count continues to rise until, with the onset of suppuration, leukocytes are withdrawn from the blood to the infected focus more rapidly than they are poured into the blood from the bone marrow. If the infective process continues to spread, this withdrawal of leukocytes from the circulation may be of sufficient extent to produce leukopenia. The curves of the leukocyte and polymorphonuclear counts in uncomplicated cases of lobar pneumonia are similar to the curves in uncomplicated cases of acute appendicitis, rising abruptly with the onset of the infection, remaining high during the acute stages of the disease and falling together to the base line as the infection subsides. In cases of lobar pneumonia complicated by empyema, the curves resemble those in acute appendicitis with abscess formation or peritonitis, as with the onset of suppuration in the pleural cavity the leukocyte count shows an abrupt fall while the polymorphonuclear factor remains elevated.

Connecticut State Medical Society Journal, Hartford

2: 523-590 (Nov.) 1938

Horace Wells and His Discovery of Anesthesia. W. R. Steiner, Hartford.—p. 525.
Hypnotism and Its Relation to Anesthesia. B. B. Raginsky, Montreal.—p. 527.
Postoperative Atelectasis. H. F. Bishop, Hartford.—p. 534.
*Some Experiences Gained in Series of 500 Epidural Blocks. B. C. Sword, New Haven, and A. E. Harrington, Milford.—p. 539.
Methods of Anesthesia for Operations About the Head and Neck. R. C. Adams, Rochester, Minn.—p. 544.
Present Status of Pentothal Sodium as an Anesthetic Agent. M. Garofalo, Hartford.—p. 550.
Role of Surgery in Treatment of Heart Disease. H. M. Marvin, New Haven.—p. 558.
Late Latent Syphilis. A. K. Poole, New Haven.—p. 569.

Epidural Block.—From an experience of 500 epidural block anesthesias Sword and Harrington conclude that the procedure can be used in most types of cases in which operation is below the diaphragm. Old age is not a contraindication. In the majority of cases adequate sedation can be produced by the proper timing of the preliminary medication. Too great a fall in blood pressure occurs if morphine, scopolamine or pentobarbital sodium is given in the usual doses an hour before the operation. The main objection to this type of anesthesia seems to be the delay it causes in a busy operating room. Poor surgical risks show a better recovery when this method of anesthesia is used.

Indiana State Medical Assn. Journal, Indianapolis

31: 593-662 (Nov.) 1938

Tuberculosis Association and the Problem of Early Diagnosis. M. A. Auerbach, Indianapolis.—p. 594.
Pulmonary Tuberculosis: The Problem of the General Practitioner. J. V. Pace, Rockville.—p. 596.
Tuberculosis in General Practice. C. J. McIntyre, Indianapolis.—p. 599.
Medical Treatment of Pulmonary Tuberculosis. J. O. Parramore, Crown Point.—p. 602.
Tuberculous Pneumonia. J. W. Strayer, Lafayette.—p. 605.
Surgical Treatment of Pulmonary Tuberculosis. J. H. Stygall, Indianapolis.—p. 609.
Tuberculosis: Where Do We Go from Here? G. C. Johnson, Evansville.—p. 612.
The Future Outlook in Tuberculosis. M. H. Draper, Fort Wayne.—p. 614.
Eventration of the Diaphragm Following Empyema: Case Report. G. A. Dickinson, Petersburg.—p. 615.
Complete Rupture of the Uterus. G. W. Gustafson and W. E. Crump, Indianapolis.—p. 616.

Johns Hopkins Hospital Bulletin, Baltimore

63: 283-348 (Nov.) 1938

Effect of Preventing Development of Hypersensitivity in Experimental Tuberculosis. R. H. Follis Jr., Baltimore.—p. 283.
Spirocheticidal Action of Bismuth Compounds on Pathogenic Spirocheta Pallida in Vitro. H. Eagle, Baltimore.—p. 305.
*Absorption and Excretion of Certain Sulfanilamide Derivatives. E. K. Marshall Jr., W. C. Cutting and W. L. Cover, Baltimore.—p. 318.
Absorption and Excretion of Sulfanilamide in Mouse and Rat. E. K. Marshall Jr. and W. C. Cutting, Baltimore.—p. 328.
*Passage of Sulfanilamide Through the Human Placenta. H. Speert, with technical assistance of Dorothea Babbitt, Baltimore.—p. 337.
Delayed Toxic Reaction to Sulfanilamide: Case Report. L. Danziger, Baltimore.—p. 340.

Absorption and Excretion of Sulfanilamide.—Marshall and his associates compared the absorption and excretion in dogs of moderately soluble sulfanilamide, easily soluble mono-ethanol sulfanilamide and slightly soluble disulfanilamide. They found that ethanol sulfanilamide is absorbed and also excreted very rapidly, while disulfanilamide is absorbed slowly and excreted rapidly in comparison with sulfanilamide. Little increased absorption occurs with a large dose of the easily insoluble compound as compared with a small one. Sulfanilamide when given in solution by mouth is absorbed much more quickly than when

given in solid form. Absorption is slight from the stomach but rapid from the intestine. Sulfanilamide derivatives do not all pass into the spinal fluid as readily as does sulfanilamide.

Passage of Sulfanilamide Through Human Placenta.—Speert studied the transmission of sulfanilamide through the human placenta. His studies confirm those of Lee, Anderson and Chen that the drug passes readily from mother to fetus. The sulfanilamide concentration of the fetal blood rapidly approaches that of the mother, equilibrium being reached within approximately five hours. This was true for both the free and the acetylated forms of the drug, a finding at variance with the results of the foregoing authors. The concentration of sulfanilamide in the amniotic fluid indicates a correspondingly free passage of the drug. Clinically, infants show no ill effects from the drug either at birth or during the neonatal period. The data presented represent the placental transmission of sulfanilamide in the human being only at term. It is entirely possible that in earlier stages of pregnancy great differences from the present observations may occur.

Journal of Bacteriology, Baltimore

36: 337-454 (Oct.) 1938. Partial Index

Apparent Oxidation-Reduction Potentials of Bright Platinum Electrodes in Synthetic Medium Cultures of Bacteria. W. E. Ward, Chicago.—p. 337.
Heat Sterilized Reducing Sugars and Their Effects on Thermal Resistance of Bacteria. J. G. Baumgartner, London, England.—p. 369.
Micro-Organism Decomposing Group Specific Substances. M. W. Chase, New York.—p. 383.
Relationships of Coliform Organisms. C. A. Stuart, A. M. Griffin and Muriel E. Baker, Providence, R. I.—p. 391.
Coliform Organisms in Certified Milk. C. A. Stuart, K. M. Wheeler and A. M. Griffin, Providence, R. I.—p. 411.
Comparative Studies on Purification of Tetanus and Diphtheria Toxins. M. D. Eaton and A. Gronau, St. Louis.—p. 423.
Oxidations Produced by Hemolytic Streptococci. E. S. G. Barron and H. R. Jacobs, Chicago.—p. 433.

Journal of Experimental Medicine, New York

68: 641-788 (Nov.) 1938

Reactions of Normal and Tuberculous Animals to Tuberculoprotein and Tuberculophosphatide. K. C. Smithburn and Florence R. Sabin, New York.—p. 641.
*Tubercular Allergy Without Infection. Florence R. Sabin and A. L. Joyner, New York.—p. 659.
*Studies on Eastern Equine Encephalomyelitis: I. Histopathology of Nervous System in Guinea Pig. L. S. King, Princeton, N. J.—p. 677.
Production by New Method of Renal Insufficiency and Hypertension in Rabbit. D. R. Drury, Los Angeles.—p. 693.
Immunologic Reactions with Virus Causing Papillomas in Rabbits: I. Demonstration of Complement Fixation Reaction: Relation of Virus-Neutralizing and Complement-Binding Antibodies. J. G. Kidd, New York.—p. 703.
Id.: II. Properties of Complement-Binding Antigen Present in Extracts of Growths: Its Relation to Virus. J. G. Kidd, New York.—p. 725.
Id.: III. Antigenicity and Pathogenicity of Extracts of Growths of Wild and Domestic Species: General Discussion. J. G. Kidd, New York.—p. 737.
Intraperitoneal and Intracerebral Routes in Serum Protection Tests with Virus of Equine Encephalomyelitis: II. Mechanism Underlying Difference in Protective Power by Two Routes. P. K. Olitsky and C. G. Harford, New York.—p. 761.
Id.: III. Comparison of Antiviral Serum Constituents from Guinea Pigs Immunized with Active or Formolized Inactive Virus. P. K. Olitsky and C. G. Harford, New York.—p. 779.

Tuberculous Allergy Without Infection.—On the basis of their studies Sabin and Joyner conclude that guinea pigs can be rendered hypersensitive to tuberculoprotein by small, repeated, intradermal injections of active tuberculoprotein. The addition of tuberculophosphatide to the protein speeds up the process of sensitization and enhances it so that the reactions become indurated and necrotic, closely simulating those of the disease. Active tuberculoproteins induce a new formation of monocytes and some epithelioid cells. The addition of phosphatide to the protein brings about a massive formation of epithelioid cells. The increase in the speed and intensity of the sensitization may be correlated with the increased cellular reaction to the mixed injections. The intradermal route is the best for these sensitizations, probably because it provides the greatest dose per cell of the sensitizing agent. The degree of sensitization artificially obtainable by the synergistic action of tuberculophosphatide and tuberculoprotein is quite comparable to the degree of sensitization naturally occurring in tuberculous animals; moreover, this degree of sensitization may be induced with amounts of the materials from the bacilli which could conceivably be present in the tissues of an infected host.

Eastern Equine Encephalomyelitis.—King studied the neuropathologic features of equine encephalomyelitis in the guinea pig. The histogenesis of the disease process is described. After peripheral inoculation the earliest detectable pathologic change is the accumulation of leukocytes within the lumen of the blood vessels and the proliferation of the vascular adventitia. This precedes the appearance of any significant perivascular cuffing and may or may not be accompanied by a few polymorphonuclear leukocytes. The typical lesion is a fairly well circumscribed focus of polymorphonuclear leukocytes accompanying the foregoing vascular changes. The leukocytes may be numerous or sparse and may or may not be accompanied by neuron destruction. The neocortices and olfactory cortices are the principal sites of predilection. A distinction between inflammatory and degenerative lesions depends on the relationship between the neuron destruction and the exudative changes. After intracerebral inoculation the inflammatory changes are much less marked than after peripheral inoculation. This is due to a different type of pathologic process. Following intracerebral inoculation there is primary destruction of neurons, involving especially the hippocampus and also large areas of the neocortex. This change, similar to ischemic necrosis, is regarded in part as a nonspecific reaction of especially vulnerable tissue.

Military Surgeon, Washington, D. C.

83: 275-400 (Oct.) 1938

Indications for and Value of Various Types of Sympathectomy. A. W. Adson.—p. 275.
Observations at the Mayo Clinic. C. L. Leedham.—p. 294.
Malaria in the Panama Canal Department, United States Army: I. Incidence of Primary Cases in 1936 and 1937. G. R. Callender and C. J. Gentzkow.—p. 299.
Low Back Pain. F. A. Jostes.—p. 316.
Chronic, Intractable Ulcerative Colitis. F. R. Sedgley.—p. 326.
Importance of Medicodental Cooperation. O. A. Oliver.—p. 329.
History of the 102d Medical Regiment New York National Guard. L. A. Salisbury.—p. 339.
Medical Field Service School, U. S. Marine Barracks, Quantico, Va. H. E. Gillespie.—p. 343.
Statistical Study of 1,781 Appendectomies in CCC Personnel of the Fourth Corps Area from 1933 to 1936, with Especial Reference to Comparative Mortality Rates. F. F. Rudder.—p. 345.

New England Journal of Medicine, Boston

219: 685-730 (Nov. 3) 1938

Relation of Dermatology to General Medicine. G. A. Dix, Worcester, Mass.—p. 685.
Lupus Erythematosus Discoides: Its Present Status with Regard to Etiology and Treatment. M. M. Tolman, Boston.—p. 688.
Are Patch Tests of Real Value in Dermatology? J. G. Downing, Boston.—p. 698.
Use of Scratch Test in Dermatology, with Special Reference to Atopic Dermatitis. J. Goodman, Boston.—p. 705.
Syphilitic Scars of the Spirit. A. W. Cheever, Boston.—p. 709.

New Orleans Medical and Surgical Journal

91: 211-270 (Nov.) 1938

Possible Role of Intestinal Toxemia in Liver Damage. A. Eustis, New Orleans.—p. 211.
Traumatic Stricture of Cervix. H. E. Miller and C. G. Collins, New Orleans.—p. 216.
Ruptured Pyosalpinx. N. J. Tessitore and J. S. Potekin, New Orleans.—p. 222.
Hyperthyroidism. R. B. Wallace, Alexandria.—p. 226.
Thrombocytopenic Purpura: Three Case Reports. J. G. Snelling, Monroe, La.—p. 231.
Determination of Vitamin C Deficiency. Grace A. Goldsmith, New Orleans, and G. F. Ellinger, Mount Vernon, Wash.—p. 237.
Ruptured Intervertebral Disk: Cause of Sciatic Pain. D. H. Echols, New Orleans.—p. 243.
*Pregnant Woman with Lobar Pneumonia, Type VIII, Cured by Specific Serum. J. H. Musser and M. J. Boggs, New Orleans.—p. 246.

Recovery from Lobar Pneumonia in Pregnancy.—Musser and Boggs report the case of a woman seven months pregnant who recovered from type VIII pneumonia after specific serum therapy was given on the second day of illness. The patient was tested for sensitivity by the conjunctival method and the reaction was negative. She was then given 10,000 units of type VIII antipneumococcus serum prepared from rabbits' serum, two hours later she was given 40,000 units intravenously,

four hours later 40,000 units, and this was repeated in another four hours. The day after the serum was administered the patient's temperature was normal, her extreme cyanosis and dyspnea, which required oxygen, had disappeared and five days later she was discharged from the hospital entirely well.

Ohio State Medical Journal, Columbus

34: 1197-1308 (Nov.) 1938

Passive Prophylaxis Against Acute Infections in Childhood. J. A. Toomey, Cleveland.—p. 1213.
Chronic Gastritis: Present Day Status: Part I. L. Schiff and S. Goodman, Cincinnati.—p. 1220.
Surgical Treatment of Diverticulitis. T. E. Jones, Cleveland.—p. 1225.
*Surgical Treatment of Epilepsy. J. P. Evans, Cincinnati.—p. 1229.
Membranes. F. S. Mowry, Cleveland.—p. 1232.
Technic for Mastoidectomies Under Local Anesthesia. M. E. Scott, Massillon.—p. 1235.
Treatment of Prenatal Syphilis. E. W. Netherton, Cleveland.—p. 1237.
Perirectal Abscesses. W. W. Green, Toledo.—p. 1245.
Gonorrheal Infection in Children Treated with Sulfanilamide: Report of Fifty Cases. J. E. Hoberg, Columbus, and L. E. Reck, Adrian, Mich.—p. 1249.
Carbon Monoxide Poisoning. H. A. Martin, Toledo.—p. 1251.

Surgical Treatment of Epilepsy.—Evans states that the first requirement of selecting cases of epilepsy for surgical intervention is that the epilepsy be due to focal lesions in the brain. It might then appear that any generalized seizure would be excluded from consideration at the outset. This, however, is not always so, for it is conceivable that a seizure firing, for example, from one of the frontal poles, might work up its abnormal cerebral rhythm in a silent area of the brain and that the seizure would then spread rapidly, firing off the entire body musculature at one time. It is the usual rule, however, that cases of generalized seizures less often prove susceptible to surgical intervention. It is essential to analyze carefully both the subjective and the objective course of events in the patient's seizure and thus sort out by detailed analysis signs which indicate the initial area of abnormal discharge. Another criterion for the selection of cases suitable for surgical intervention is the pneumo-encephalographic evidence of focal damage. A third criterion is the finding at the site of suspected pathologic change variations of electrical potential characteristic of epileptic discharge. Use of this method depends on further elaboration of the methods of electro-encephalography. However, before radical excision of the suspected area is undertaken, a fourth criterion should be met—the production of a characteristic seizure by carefully controlled electrical stimulation of the exposed cortex. Finally, any patient should have, before operation is seriously considered, a thorough trial of phenobarbital or other sedative therapy, partly to avoid unnecessary operation, partly to prove that any postoperative sedation employed is not the cause of postoperative improvement rather than the operation itself. The aim of operative intervention is to excise the damaged area of the brain, leaving a lesser degree of damage than was caused by the original injury. This involves an understanding of the anatomic arrangement of the blood vessels and of the physiology of collateral circulation. The author concludes that the results of radical excision of cerebral cicatrix are, in his opinion, such as to justify further intelligent and critical pursuit of the problem.

Physiological Reviews, Baltimore

18: 481-596 (Oct.) 1938

Formation of Egg of Domestic Fowl. R. M. Conrad and H. M. Scott.—p. 481.
Application of Law of Chemical Equilibrium (Law of Mass Action) to Biologic Problems. F. C. McLean, Chicago.—p. 495.
Plant Growth Hormones. K. V. Thimann, Cambridge, Mass., and J. Bonner, Pasadena, Calif.—p. 524.
Physiologic Effects of Small Amounts of Lead: Evaluation of Lead Hazard of the Average Individual. A. S. Minot, Nashville, Tenn.—p. 554.
Factors Concerned in Duration of Pregnancy. F. F. Snyder, Baltimore.—p. 578.

Public Health Reports, Washington, D. C.

53: 1907-1960 (Oct. 28) 1938

Disabling Sickness Among Male Industrial Employees During the Second Quarter and the First Half of 1938. W. M. Gafafer and Elizabeth S. Frasier.—p. 1910.
Studies of Sewage Purification: VIII. Observations on Effect of Variations in Initial Numbers of Bacteria and of Dispersion of Sludge Flocs on Course of Oxidation of Organic Material by Bacteria in Pure Culture. C. T. Butterfield and Elsie Wattie.—p. 1912.

Radiology, Syracuse, N. Y.

31: 391-520 (Oct.) 1938. Partial Index

Roentgen Kymography as Diagnostic Aid. P. Stumpf, Munich, Germany.—p. 391.
Roentgenologic Diagnosis of Tumors Involving the Sacrum. J. D. Camp and C. A. Good Jr., Rochester, Minn.—p. 398.
Roentgenographic Demonstration of Pulmonary Veins. B. S. Epstein, Brooklyn.—p. 418.
Emphysematous Cholecystitis and Pericholecystitis. E. A. Schmidt, Denver.—p. 423.
*Variations in Position of Normal Coccyx. L. J. Friedman and C. Stein, New York.—p. 438.
Osseous Growth and Development. E. C. Vogt and Vernette S. Vickers, Boston.—p. 441.
Coarctation of the Aorta: Three Cases with Necropsy Findings in One. T. B. Weinberg and C. Gartenlaub, New York.—p. 445.
Effect of Radiation Applied Directly to the Brain and Spinal Cord: I. Experimental Investigations on Macacus Rhesus Monkeys. L. M. Davidoff, C. G. Dyke, C. A. Elsberg and I. M. Tarlov, New York.—p. 451.
Concerning Diagnosis of Lesions in Lower Spinal Canal. J. C. Bell and R. G. Spurling, Louisville, Ky.—p. 473.

Variations in Position of Normal Coccyx.—Friedman and Stein observed the position of the coccyx in 100 adults, chosen at random, who were free of any symptoms referable to the spine and who had no history of trauma to the sacrum or coccyx. Roentgenograms were taken in the anteroposterior and lateral positions. Angulations (from 5 to 65 degrees) at the sacrococcygeal and first coccygeal articulations are to be found in the normal spine. The variation may occur either in the transverse or sagittal plane and, more rarely in both.

Rocky Mountain Medical Journal, Denver

35: 833-936 (Nov.) 1938

Roentgen Diagnosis of Acute Abdominal Conditions. L. G. Rigler, Minneapolis.—p. 850.
Surgical Complications Resulting from Presence of Heterotopic Tissue in Meckel's Diverticulum. W. C. Black and G. B. Packard, Denver.—p. 859.
Acute Lymphocytic Meningitis. P. A. Draper, Colorado Springs, Colo.—p. 863.
Mrs. Brown Has Boy in Spite of Lots of Things. C. B. Ingraham, Denver.—p. 867.

South Carolina Medical Assn. Journal, Greenville

34: 279-302 (Nov.) 1938

Serum Therapy in Lobar Pneumonia. W. H. Kelley, Charleston.—p. 279.
Difficulties in Abdominal Diagnosis in Children—Illustrative Cases. D. Jennings, Bennettsville.—p. 282.
Retropharyngeal Abscess. C. W. Evatt, Charleston.—p. 287.

Surgery, St. Louis

4: 649-808 (Nov.) 1938

Treatment of Paralytic Bladder in Cases of Spinal Cord Injury. F. Hinman, San Francisco.—p. 649.
Tumors of Kidney Which Invade Inferior Vena Cava: Report of Seven Cases. J. H. Tillisch, H. C. Habein and J. C. Henthorne, Rochester, Minn.—p. 663.
Role of Urea-Splitting Organisms in Formation of Certain Types of Stones in Urinary Tract. E. Burns, New Orleans.—p. 673.
*Use of Vitamin B_1 in Preoperative Preparation of Hyperthyroid Patient. W. D. Frazier and I. S. Ravdin, Philadelphia.—p. 680.
Nonoperative Treatment of Perforated Gastric Ulcer with Generalized Peritonitis by Continuous Gastric Siphonage. P. Nagle, Oklahoma City.—p. 687.
Acidity of Gastric Contents After Excision of Antral Mucosa. E. B. Lewis, Rochester, Minn.—p. 692.
Wandering Spleen with Torsion of the Pedicle: A Patient Treated by Splenectomy with Alarming Events During Convalescence. P. E. Truesdale and D. Freedman, Fall River, Mass.—p. 700.
Endometrial Tumors in Postcesarean Abdominal Laparotomy Scars. P. A. Kaufman and A. O. Wilensky, New York.—p. 708.
Etiology of Vasomotor and Nutritional Changes Following Peripheral Nerve Section. L. N. Atlas, Cleveland.—p. 718.
New Modification of Subarachnoid Alcohol Injection for Bilateral Blocking of Lower Sacral Nerves in Intractable Pain of Pelvic Viscera. J. C. White, Boston.—p. 722.
Acute Aerobic (Nonputrid) Abscess of Lung. H. Neuhof and A. S. W. Touroff, New York.—p. 728.
*Incidence of Air-Borne Bacteria in the Major Surgery of Multnomah County Hospital. O. M. Nisbet and J. W. Brooke, Portland, Ore.—p. 755.
Osteopsathyrosis: Report of Three Cases. K. M. Lippert, Richmond, Va.—p. 762.
Rupture of Esophagus in a Child Two Years of Age, with Recovery. C. D. Benson and G. C. Penberthy, Detroit.—p. 777.

Preoperative Vitamin B_1 and Thyroidectomy.—The evidence that a vitamin B complex or B_1 deficiency may play a part in the production of certain of the gastrointestinal disturbances, especially the anorexia often exhibited by the hyper-

thyroid patient, is discussed by Frazier and Ravdin. Several years ago they began the use of a vitamin B complex extract in patients suffering from hyperthyroidism. The patients were given large amounts of the extract with no other therapy during the period of observation. Although the basal metabolic rate was not reduced any more than in a control group, the general condition of the patients given the vitamin was better than the control group. The beneficial effects of the vitamin were compared with that of twenty-eight patients similarly treated in every respect except that no vitamin B was administered. The routine preoperative treatment was complete bed rest except for two hours daily, high caloric, high carbohydrate diet consisting of from 3,000 to 4,000 calories daily, from 5 to 10 minims (0.3 to 0.6 cc.) of saturated solution of potassium iodide three times a day, 0.65 Gm. of sodium bromide three times a day and 1½ grains (0.1 Gm.) of phenobarbital nightly. The fifty vitamin treated patients received in addition to the foregoing regimen 10 mg. of crystalline vitamin B_1 hypodermically every other day and 10 Gm. of brewers' yeast daily by mouth. Improvement in the vitamin treated patients, over the control group, occurred to the degree that the pulse rate was reduced during the period of preparation, patients gained weight and their appetite was increased and the length of time required for adequate preoperative preparation was shortened. These results are in agreement with the known effect of vitamin B_1 on the cardiovascular and gastrointestinal systems, if some degree of vitamin B deficiency exists. The two series of patients showed no significant differences in the lowering of the basal metabolic rate before operation or in the severity of the postoperative reaction. When improvement was noted in the vitamin treated series it was most marked in the more toxic group.

Air-Borne Bacteria.—Nisbet and Brooke found that the number of air-borne bacteria in the major surgery rooms of Multnomah County Hospital is roughly proportional to the number of persons present and to the activity on the floor proper of the surgery. The greatest proportionate rise in incidence is manifested by the streptococci and Staphylococcus albus. The organisms showing this rise are acknowledged to be common inhabitants of the nasopharynx. The estimated number of bacteria falling per hour on a sterile operating field compares unfavorably with similar figures obtained in other hospitals. The assumption that this increase is due in part to the agitation of air currents caused by the passage of the operating room assistants does not appear to be unwarranted. It is possible that some bacteria are carried into the surgery by the footwear.

Tennessee State Medical Assn. Journal, Nashville

31: 381-424 (Oct.) 1938

*Sterilization of the Female by Cauterization of Uterine Cornu. C. G. Bowers and Margaretta Keller Bowers, Lyles.—p. 381.
Comparative Aspects in Treatment of Syphilis. E. R. Hall, Memphis.—p. 388.
The Changing Pediatric Picture. E. Rosamond, Memphis.—p. 393.

Sterilization of the Female.—The Bowerses present a method for the sterilization of women for which hospitalization is not necessary. The procedure can be carried out in the office as it is only slightly more disturbing than cervical cauterization. After determining the necessity for sterilization, the patient is requested to be at the office a week or ten days after her regular menstrual period. She is instructed to take a copious douche of warm soda water an hour before her appointment. Following pelvic palpation she is left in the lithotomy position and a Sims speculum is introduced. The vagina and vaginal wall are thoroughly swabbed with a suitable antiseptic. The plug of mucus occluding the os is removed and the cervical canal is cleaned. A lip of the cervix is grasped with a tenaculum, and a catheter to which is attached a syringe with 10 cc. of radiopaque oil is inserted until its tip passes the internal os and the rubber olive fits snugly into the canal. The oil is injected slowly. The injection is discontinued, but the catheter is retained in position to prevent outflow of oil. A roentgenogram is taken and immediately developed, outlining the cavity of the tubes and uterus. The electrode employed is about 9 inches long and one-fifth inch in diameter; the distal end is semiflexible and is tipped with a small conical coil of platinum wire. Proximally there are two leads for electrical connections. The cauterizing coil at the tip is of platinum wire. To bring the cautery to a "cherry red" in air it was found that 8 ± 0.1 amperes was required, corresponding to a consumption of 0.96 watt. The cautery electrode is then introduced, following the route previously outlined by the sound. Its active tip is snugly fitted into the uterine horn and by touch on its shank it is determined to be in contact with the mucosa on all sides. The current is then turned on for about forty-five seconds; meanwhile the active tip is given a slow rotary motion of a single revolution. This movement of the cautery tip prevents too deep a burn in one spot in the cornu and it causes the cauterization to be distributed about the entire funnel surface of the cornu, causing destruction of all the mucosa in this area and giving assurance against fistulous formation. It is important that the zone of coagulation extend into the muscular wall of the uterus, as it is here that the contracture is produced. The opposite side is similarly cauterized and a gauze sponge is left in the vagina to absorb the oily and sanguineous exudate, which the patient is instructed to remove when she returns home. Within a few days following the treatment there will be a serosanguineous discharge for a week or so which may necessitate a daily cleansing douche. Six weeks after the cauterization the patency of the tubes is checked either by air insufflation or roentgenologically. If the tube is closed, the cornu will be seen to be dome shaped and no oil will enter the tube. Contraindications for carrying out the procedure include any active infection of the genito-urinary system or any chronic infection of the tubes or uterus. Patients with malignant growths, fibroids, polyps and endometritis should not be treated with the cautery electrode. Of a series of twelve patients, six were cauterized once, five were cauterized twice and one was cauterized three times before closure was complete.

Virginia Medical Monthly, Richmond

65: 651-722 (Nov.) 1938

A Few Leaves from the Diary of That Fast Disappearing Representative of the Genus Homo, the Country Doctor. G. F. Simpson, Purcellville.—p. 651.
Pioneering in Health—1908 to 1910. R. K. Flannagan, Richmond.—p. 655.
Painless Childbirth Made Safe with Paraldehyde. S. M. Dodek, Washington, D. C.—p. 661.
Current Methods of Treating Mental Cases in Virginia. H. C. Henry, Richmond.—p. 664.
Important Points to Be Remembered About Crossed Eyes: Lantern Demonstrations. J. A. Pilcher Jr., Roanoke.—p. 667.
Syphilis in Childhood. Louise Fry Galvin, Richmond.—p. 670.
The Physician's Role in Adoption. Lois Benedict, Roanoke, and B. B. Jones, Richmond.—p. 674.
*Eleven Cases of Toxemia of Pregnancy Treated with Progesterone. W. McMann, Danville.—p. 676.
Use of Insulin in Certain Psychiatric Disorders. R. M. Crowley, Rockville, Md.—p. 678.
Hemorrhage from Upper Gastrointestinal Tract: Its Medical Management: A Review. J. F. Waddill, Norfolk.—p. 682.
The Management of the Heart in Pregnancy. E. Podolsky, Brooklyn.—p. 686.

Toxemia of Pregnancy Treated with Progesterone.—McMann used a preparation of corpus luteum hormone in the treatment of eleven cases of toxemia of pregnancy. No other treatment was given. Labor was induced when the prognosis seemed precarious. The final results were disappointing. There were three absolute failures, two were questionable and six patients seemed to respond to treatment. The response, however, was greater than when the dehydration principles of Arnold and Fay, coupled with rest and strict attention to diet, are used.

West Virginia Medical Journal, Charleston

34: 485-532 (Nov.) 1938

Recent Advances in Treatment of Pneumonia. D. A. MacGregor, Wheeling.—p. 485.
Statistics on Lobar Pneumonia, from a West Virginia Hospital. W. L. Cooke, Charleston.—p. 494.
The Art of Diagnosis. J. C. Gittings, Philadelphia.—p. 497.
Syphilis in Mining Communities. W. P. Bittinger, Summerlee.—p. 506.
Pulmonary Suppuration. L. H. Clerf, Philadelphia.—p. 513.
Local Anesthetic Crises in Rhinolaryngology. Sobisca S. Hall and H. V. Thomas, Clarksburg.—p. 516.
Rat-Bite Fever: Case Report. J. E. Fisher, New Cumberland.—p. 521.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Physical Medicine, London

1: 331-366 (Oct.) 1938

Rheumatism and Electrotherapy. W. Beaumont.—p. 332.
Chronic Arthritis in Women. C. A. Robinson and V. C. Robinson.—p. 340.
Occupational Therapy in Treatment of Arthritis. W. S. C. Copeman.—p. 350.
Diet in Rheumatic Diseases. J. A. Nixon.—p. 353.

British Journal of Surgery, Bristol

26: 217-456 (Oct.) 1938. Partial Index

Abdominal Injuries and Their Recipients. G. Gordon-Taylor.—p. 217.
Transsphenoidal Decompression for Pituitary Adenoma. G. Phillips.—p. 242.
Investigation into Condition of Bladder Mucosa in Relation to Stone Formation. J. Gray.—p. 259.
Saccular Aneurysms of Internal Carotid Artery in Cavernous Sinus. G. Jefferson.—p. 267.
Carcinoid Tumors of Appendix. T. Moore.—p. 303.
*Endothelioma of Pleura: Two Cases. N. R. Barrett and J. St. C. Elkington.—p. 314.
Operation for Recurrent Dislocation (Subluxation) of Sternoclavicular Joint. A. S. B. Bankart.—p. 320.
Nerve Supply of Gastro-Esophageal Junction. G. A. G. Mitchell.—p. 333.
Extradural Hemorrhage. K. G. McKenzie.—p. 346.
Spinal Epidural Suppuration, with Special Reference to Osteomyelitis of Vertebrae. F. A. R. Stammers.—p. 366.
Recurrent Dislocation of Shoulder: A Plea for Simple Operation. E. W. H. Groves.—p. 375.
*Granulomatous Ulcers Resembling Tuberculous Ulcers of the Stomach. M. G. Kini and M. Narasimha Rao.—p. 379.
Simultaneous Perforation of Multiple Peptic Ulcers. W. E. Austin.—p. 387.
Surgical Treatment of Obstructive Jaundice in Pancreatic Disease. J. Fraser.—p. 393.
Behavior of Blood Volume in Intestinal Obstruction and Strangulation. I. Aird.—p. 418.
Sarcoma of Intestine in Children. A. Simpson-Smith.—p. 429.

Endothelioma of Pleura.—There is no general agreement that endothelioma of the pleura exists as a pathologic or a clinical entity. Barrett and Elkington do not enter into this controversy but rather point out and explain some physical signs which they found in two cases of diffuse new growth of the pleura. In both cases a careful postmortem examination was made. In neither was a primary tumor demonstrable in the bronchial tree nor was there any evidence of lymphatic invasion in spite of the fact that the growths were extensive. In the second case malignant cells were found in the sputum before death, and these were diagnosed as from an endothelioma. At the postmortem examination of this case it was obvious that the malignant tissue was invading the bronchi from without, and paraffin sections showed the mucosa intact in places in which collections of malignant cells had penetrated between the cartilaginous rings and extended along the submucosa. The fact that malignant cells were ultimately demonstrable in the sputum is not necessarily an argument in favor of the suggestion that this was a primary bronchial growth. From the clinical point of view, both these tumors gave physical signs which were difficult to interpret in the early stages. In each case the respiratory signs pointed to a marked, progressive and diffuse thickening of the pleura, with little evidence of involvement of the lung itself. The nervous signs were strikingly similar. They consisted of wasting and complete paralysis of certain of the intercostal muscles on one side and also of the upper segment of the abdominal recti and oblique muscles. In each case the diaphragm on that side was immobile.

Granulomatous and Tuberculous Gastric Ulcers.—Kini and Narasimha Rao state that when extensive shallow ulcers with undermined edges occur in the pyloric region it becomes difficult to differentiate them from malignant disease of the pyloric antrum. After gastrectomy one of the three ulcers in their series, which appeared to the naked eye to be typically tuberculous, failed to show on microscopic examination any evidence of tuberculosis (case 3). Case 1 was diagnosed as a case of malignant disease and a gastrectomy was performed. It was only after gastrectomy that the ulcer was found to be granulomatous, resembling a tuberculous ulcer, which on microscopic examination it was suspected to be. In case 2 no gastrectomy could be performed, as the general condition of the patient was poor. While gastro-enterostomy was being performed, a good view of the ulcer could be obtained through the stoma. It resembled the ulcer in case 1. The gland removed for biopsy was suspected to be tuberculous on microscopic examination. Case 3 resembled the first in all its aspects, but on histologic examination there was no evidence of tuberculosis in the sections examined. A gastrectomy was performed.

British Journal of Tuberculosis, London

32: 205-260 (Oct.) 1938

What Can Be Done to Prevent the Tuberculous Patient from Relapsing? G. C. Williams.—p. 208.
Id. H. G. Trayer.—p. 211.
The Prevention of Relapse in Cases of Pulmonary Tuberculosis. F. H. Young.—p. 216.
The Prevention of Relapse in the Tuberculous Patient: An After-Care Problem. K. N. Irvine.—p. 221.
What Can Be Done to Prevent the Tuberculous Patient from Relapsing? A. M. Cooke.—p. 225.
Pleural Perforation in Pulmonary Tuberculosis: Character of Pleural Exudate: Diagnosis of Perforation by Gas Analysis. H. Harpöth and U. Gad.—p. 228.
Tomography. H. Roche.—p. 236.

Journal of Laryngology and Otology, London

53: 625-684 (Oct.) 1938

*Observations on the Pathology of Ménière's Syndrome. C. E. Hallpike and H. Cairns.—p. 625.
Osteoclastoma of Frontal Bone in Hyperparathyroidism. R. P. Mathers and D. F. Cappell.—p. 656.

Pathology of Ménière's Syndrome.—Hallpike and Cairns describe the microscopic changes in the temporal bones of two patients with Ménière's syndrome. In each of these the affected temporal bone showed a gross distention of the endolymphatic system together with degenerative changes in the sensory elements. A possible explanation of this distention is suggested by the absence in both patients of the normal area of perisaccular connective tissue around the saccus endolymphaticus. A possible mechanism is further suggested whereby the microscopic changes may be correlated with the clinical features of the disease.

Journal of Physiology, London

94: 1-186 (Oct. 14) 1938. Partial Index

Factors in Sexual-Skin Edema. Olive E. Aykroyd and S. Zuckerman.—p. 13.
Effect of High Doses of Androgenic Substances on Weights of Testes, Accessory Reproductive Organs and Endocrine Glands of Young Male Guinea Pigs. A. C. Bottomley and S. J. Folley.—p. 26.
Influence of Glycotropic (Anti-Insulin) Factor of Anterior Hypophysis on Insulin Sensitivity of Hypophysectomized Rabbit. W. H. Newton and F. G. Young.—p. 40.
Undernutrition and Liver Fat. C. H. Best and Jessie H. Ridout.—p. 47.
Electrical Activity of Cerebellum and Its Functional Significance. R. S. Dow.—p. 67.
Action of Ephedrine. J. H. Gaddum and H. Kwiatkowski.—p. 87.
*Chloride Content of Blood Serum and Aqueous Humor: Its Relation to Glaucoma and to Formation of Intra-Ocular Fluid. T. H. Hodgson.—p. 118.
Water Balance and Blood Changes Following Posterior Pituitary Extract Administration. E. C. Dodds, S. H. Liu and R. L. Noble.—p. 124.
Action of Nicotine on Spinal Cord. A. Schweitzer and S. Wright.—p. 136.
*Absorption and Excretion of Iron Following Oral and Intravenous Administration. R. A. McCance and E. M. Widdowson.—p. 148.
Liberation of Acetylcholine by Perfused Superior Cervical Ganglion. F. C. MacIntosh.—p. 155.
Functional Impairment of Anterior Pituitary Gland Produced by Synthetic Estrogenic Substance 4: 4' Dihydroxy-α: β-Diethylstilbene. R. L. Noble.—p. 177.

Chloride Content of Blood Serum and Aqueous Humor.—Hodgson determined the chloride content of the aqueous humor and blood serum of man and dogs by the ultramicro silver iodate method. The values for a group of nonglaucomatous human beings averaged, in millimols per liter, aqueous 124.3, serum 105.1. There was no significant difference in the values obtained in cases of primary chronic glaucoma with high intraocular tension in which the average values were 126.3 for aqueous and 106.5 for serum. Normal unanesthetized dogs gave average values of 127.6 and 109.1, respectively. The high values

obtained for aqueous chloride show that there is no Donnan equilibrium for this ion between the blood and the aqueous humor, so that the latter cannot be regarded as a dialysate.

Intestinal Absorption and Excretion of Iron.—McCance and Widdowson discuss experiments planned to determine whether or not the intestine of a normal human being can excrete iron and by so doing regulate the amount of iron in the body. The investigation consisted of three stages: diets containing daily from 5.9 to 8.6 mg. of iron, from 12 to 16 mg. of iron and from 7.6 to 11.7 mg. in addition to 7 mg. of iron intravenously. Within the limits of experimental error none of the injected iron was excreted into the gastrointestinal tract. About 1.4 per cent of it was excreted in the urine, but it is believed that this is of no practical significance in iron metabolism. The results are considered to confirm the theory that the intestine has no power of regulating by excretion the amount of iron in the body. The three normal women were not in positive iron balance in their intermenstrual periods. It would be interesting to know at what time during the menstrual cycle these women absorbed the iron necessary to make good their loss.

J. Royal Inst. Public Health and Hygiene, London

1: 695-758 (Sept.) 1938

*Influences Which Undermine the Health of Women. A. Bourne.—p. 705.
The General Practitioner and Tuberculosis. K. McFadyean.—p. 712.
Some Experiences of Slum Clearance Procedure in Manchester. A. M. M. Grierson.—p. 724.
Postural and Occupational Factors in Rheumatic Pain. A. Wesson.—p. 733.
Essentials of Nutrition in Infants and Toddlers. B. E. Myers.—p. 736.

1: 759-822 (Oct.) 1938

Changing Views as to Spread of Infection. C. O. Stallybrass.—p. 769.
Id. H. G. Smith—p. 781.
Tuberculosis in Relation to the Pneumoconioses. J. V. Sparks.—p. 790.
Incidence and Significance of "Growing Pains" in Children and Adolescents. J. C. Hawksley.—p. 798.
Heart Disease and Pregnancy. J. W. Brown.—p. 806.
Respiratory Diseases in Children. W. Pearson.—p. 811.

Health of Women.—Bourne states that a great volume of the minor but chronic ill health of women is due not so much to the major difficulties or injuries of reproduction or even to the peculiar susceptibility of the pelvic organs to disease but to the wearing influence of a mass of minor worries incidental to their domestic and family life. Two main influences may affect the spinster's health. The first, a deep disappointment of the maternal instinct coupled with an underlying fear of economic insecurity, is liable to express itself physically in neurosis. The author believes that the majority of women who have not found a mate, and who have no absorbing work or object on which to exert their desire for service, do suffer in a way that will ultimately express itself physically. In the second influence it is probable that the exclusion from activity of the large element of a woman's physiologic function, as represented by her sexual organs, reacts on those organs and also on the rest of her body. It is difficult to believe that the endocrine system, so important a part of a woman's economy, can fail to suffer some impairment if the major portion of its function has never been used.

Journal of Tropical Medicine and Hygiene, London

41: 325-340 (Oct. 15) 1938

Classification of Certain Groups of Intestinal Bacteria Belonging to the Family Bacillaceae: Tribe Ebertheae and Tribe Encapsulateae. A. Castellani.—p. 325.
Mycotic Urethritis: Contribution to Study of Nongonorrheal Urethritis. C. Pisacane and A. Coppolino.—p. 332.

Lancet, London

2: 929-982 (Oct. 22) 1938

The State and Medical Research. E. Mellanby.—p. 929.
Meningococcic Meningitis Treated with Proseptasine and Soluseptasine: Record of Nine Cases. R. H. Hannah and F. G. Hobson.—p. 937.
*Slowly Fatal Pulmonary Embolism. R. Pilcher.—p. 942.
Meningo-Encephalitis Complicating Herpes Zoster. J. H. Biggart and J. A. Fisher.—p. 944.
Severe Initial Deafness as a Sign of Acute Mastoiditis. N. Asherson.—p. 946.

Slowly Fatal Pulmonary Embolism.—Pilcher describes a form of fatal pulmonary embolism in which death comes slowly and suggests that such cases should be treated surgically. Four cases are reported, the cause of death being progressive cardiac failure of acute onset. In two cases embolectomy was attempted, but evidently too late. Embolectomy is suggested as the proper treatment in cases in which improvement does not occur. It should be performed two or three hours after the onset of the illness.

Archives des Maladies de l'Appareil Digestif, Paris

28: 793-912 (Oct.) 1938

Perforation of Cancer of Esophagus into Trachea and Bronchi. A. Cain, R. Cattan and H. Silorav.—p. 793.
*Value of Atropine Paralysis During Examination of Digestive Tract. A. Bernard and H. Monnier.—p. 806.
Gastric Syphilis of Pseudoneoplastic Form: Clinical and Radiologic Study. H. Marc and Sirc.—p. 813.
Cancer of Small Intestine. J. M. Noothoven Van Goor.—p. 820.

Atropine Paralysis During Examination of Digestive Tract.—Bernard and Monnier employed duodenal dilation by injection of atropine in all roentgenologic examinations of the digestive tract. The technic is as follows: At first the roentgenologic examination of the stomach is made according to the customary method; that is, a series of roentgenograms is made while the patient is standing and reclining. This procedure is followed by the subcutaneous injection of 1.5 mg. of neutral atropine sulfate, and from ten to twenty minutes later a new series of roentgenograms is made while the patient is in the erect and then in the reclining posture. Apart from a certain dryness of the oral mucosa in some instances the authors did not observe any inconvenience from this method. They employed it in seventy-six cases. Summarizing their observations, they state that the injection of atropine in the course of the roentgenologic examination of the digestive tube paralyzes and dilates the stomach, the pylorus, the duodenum, the jejunum and the colon. The transit of barium is retarded and the different organs are well filled and are in an optimal condition of stability for the x-ray film to record their pathologic deformities. Every parietal lesion, neoplasm, ulcer or condition of perigastritis remains uninfluenced by atropine. Consequently the absence of atropine paralysis of a segment of the digestive tube is an indication of an organic lesion. On the other hand, the deformities which disappear under the action of atropine can be considered as of a spasmodic nature. Thus the method permits a definite differentiation between functional and organic disorders. The atropine method brings into evidence more clearly neoplastic lacunas, gastroduodenal ulcers, diverticula and duodenal malformations. Moreover, it involves no danger and merits to be introduced into routine roentgenologic practice.

Journal de Médecine de Lyon

19: 591-622 (Oct. 20) 1938

*Curves of Sedimentation and of Serologic Reactions in Pulmonary Tuberculosis Treated by Pneumothorax: Prognostic Significance. P. Courmont and J. Moulinier.—p. 591.
Ascorbic Acid (Vitamin C) and Tuberculosis. A.-A. Policard.—p. 611.

Sedimentation and Serologic Reactions in Pulmonary Tuberculosis.—Courmont and Moulinier point out that the prognosis of pulmonary tuberculosis must be based on the serologic reactions, especially on the agglutinating power, the deviation of the complement and the bactericidal power in comparison with the clinical factors and with other reactions such as Vernes' resorcinol flocculation and the sedimentation speed. The demonstration of the value of these tests and especially their curve throughout the course of disease is simple in the acute, localized forms which are rapidly cured by pneumothorax treatment; conversely the prognosis is facilitated by these serologic curves. The authors cite the serologic curves of twenty-seven patients who were treated with pneumothorax. In fifteen only the curve of the sedimentation speed was investigated, but in the other twelve all five reactions were studied and especial attention was given to the comparison of the sedimentation speed and the agglutinating power. Some cases were observed for several years, the tests being made frequently, in many instances at monthly intervals, because the prognosis of tuberculosis is estimated in years. Isolated figures of the reactions have less value than the curves, yet an increase in the sedimentation speed and in Vernes' resorcinol reaction has an unfavorable significance at the time they are observed, whereas an

increase of the agglutinating power and of the bactericidal power is a favorable sign. The patients with pneumothorax who have a high agglutinating power are nearly always cured. The curves plotted on the basis of repeated tests and especially their comparison are of especial value. The curves of the sedimentation speed and of Vernes' resorcinol reaction have an analogous significance. They are elevated in the grave periods and at the time when complications develop; they decrease at the time of cure. Their prognostic significance is slight, because it is limited to the present time. The curves of the bactericidal power and especially of the agglutinating power are more important. Their progressive elevation signifies an excellent prognosis; on the other hand, if they are low, and especially if they decrease in the course of pulmonary tuberculosis and of pneumothorax therapy, the prognosis is unfavorable; that is, a fatal outcome may follow within several months. The serologic tests must be evaluated in connection with the clinical, roentgenologic and bacteriologic factors; they are not only helpful in fixing the prognosis but are also valuable in making decisions regarding the conduct and cessation of pneumothorax therapy and in deciding certain surgical interventions (section of adhesions, thoracectomy and so on). The easiest and most demonstrative of the serologic tests for the practice are the sedimentation speed and the agglutinating power, the latter being the most valuable. The comparison of their curves gives the best results, the sedimentation speed indicating the severity of the infection and the agglutinating power the defense of the organism.

Journal de Radiologie et d'Electrologie, Paris

22: 481-528 (Oct.) 1938. Partial Index

Secondary Electromotor Phenomena of Nerves. A. Strohl and A. Djourno.—p. 481.
*Anomalies of Vertebral Articular Processes. F. Willemin and M. Cantagrill.—p. 490.
Rapid Evolution of Pulmonary Cyst with Formation of Roentgenograms of Detachment. Brun, Jaubert de Beaujeu and Bège.—p. 495.
Role of Lung and of Pleura in Visibility of Aorta on Transverse Roentgenograms. R. Kirsch and E. Arnold.—p. 501.
Esophageal Diverticulum: Case. Estève.—p. 505.

Anomalies of Vertebral Articular Processes.—Willemin and Cantagrill call attention to the difficulties that are encountered by the roentgenologist in the interpretation of spinal roentgenograms. They cite a case in which an anomaly of vertebral articular processes existed which, although rare, may be of great medicolegal significance. The anomaly consists in accessory articular processes on the vertebrae, and the division in the continuity at the level of the vertebral articular processes may lead to confusion with fractures of the articular processes. The patient whose history is reported had accessory articular processes on the second and third lumbar and on the first sacral vertebrae. Following a detailed description of the roentgenologic aspects, the authors review the recent literature on these vertebral anomalies, giving special attention to Wilbur Bailey's report (THE JOURNAL, Jan. 23, 1937, p. 266). Bailey found nineteen cases of this anomaly in the literature, six of which presented bilateral lesions. The authors, in addition to the case which they describe and in which the anomaly was detected on three vertebrae, observed another case with an isolated accessory articular process. After citing other opinions on the incidence of the accessory vertebral articular processes, they point out that these abnormal centers of ossification are usually found on the inferior articular processes and that they are exceptionally rare on the superior articular processes.

Presse Médicale, Paris

46: 1569-1592 (Oct. 26) 1938

Pancreas of Tuberculous Patients. M. Loeper and R. Lesobre.—p. 1569.
*Treatment of Male Gonorrheal Urethritis. P. Durel.—p. 1571.

Treatment of Gonorrheal Urethritis. — Durel discusses the use of various sulfanilamide preparations in the treatment of gonorrheal urethritis. For the treatment of subjects who are not benefited by the local treatment of gonorrheal urethritis he suggests three different possibilities. First he mentions the administration of large doses of 1162 F (p-aminophenylsulfanilamide), saying that he has given 4 Gm. a day for five days, 3 Gm. a day for five days and 2 Gm. a day for five days. He emphasizes that this posology requires careful supervision and he does not advise it for routine use. A second possible treatment is the combination of 1162 F in weak doses and 40 R. P. (soluseptazine, that is, disodium-p-(gamma-phenylpropylamino) benzenesulfonamide-alpha-gamma disulfonate. The 1162 F is given for seven days in daily doses of 2 Gm., and 20 cc. of soluseptazine is given daily by intramuscular injection. This treatment may cause slight complications and the author does not consider it of great practical interest. The third method suggested is the use of sulfanilamide-pyridine. Following a description of its formula and its behavior in animals, the author describes the clinical results obtained with it. By one method the patient is given 13 Gm. of the medicament in the form of tablets over a period of eight days (two days 3 Gm. each, two days 2 Gm. each, two days 1 Gm. each and two days 0.5 Gm. each). The second method provides 18 Gm. in nine days (3 Gm. for three days, 2 Gm. for three days and 1 Gm. for three days). The third method provides 20 Gm. in eight days (4, 3, 2, and 1 Gm. for two days each). The second type of dosage seems to be suitable in the majority of cases but the author thinks that the future will doubtless modify these methods. Discussing the results obtained with sulfanilamide-pyridine he states that in acute gonorrheal urethritis in males more than 80 per cent of cures were obtained. Of the prolonged cases of urethritis about 70 per cent were cured. In women with metritis of the cervix the results have not been established as yet, but they seem superior to those obtained with other sulfanilamide preparations.

Schweizer Archiv f. Neurologie u. Psychiatrie, Zurich

42: 1-208 (No. 1) 1938. Partial Index

*Little's Disease and Epilepsy. M. Biro.—p. 1.
Individual Preparation for Collective Occupational Therapy in Patients with Severe Chronic Schizophrenia. M. Boss.—p. 15.
Action of Insulin on Normal Organism. J. Druey.—p. 27.
After-Examinations of Patients with Dementia Paralytica Who Underwent Malaria Therapy. F. Escher.—p. 37.
Sources of Querulity. A. Kielholz.—p. 58.
Determination of Tryptophan in Cerebrospinal Fluid and Its Results. M. Kraus and K. Mezey.—p. 77.
Appearance of Schizophrenic Exacerbation After Psychic Trauma. R. Mayer.—p. 88.

Little's Disease and Epilepsy.—Biro directs attention to the fact that epileptic attacks develop as accompanying symptoms of various disorders. He investigated the epileptic attacks that occur in patients with Little's disease. He says that not all convulsive attacks that occur during Little's disease can be regarded as epileptic but that attacks of an epileptic character do occur in this disease. He observed them in ten of thirty-five patients with Little's disease. The attacks usually developed during the early part of the disease. In some of the cases they preceded the other symptoms by from 3.6 to ten months, in others by only one or two days and in still others they appeared simultaneously with the symptoms of the disease. Irrespective of their time of appearance, they ceased in some of the patients during the further development of the disorder; in others they continued, with intervals, for weeks, months or years. The fact that epilepsy appears in the form of attacks proves that physiologic secondary effects are involved. Endocrine disturbances in women, in whom the attacks recur monthly, and disturbances in the intracranial pressure occasionally make it possible to detect a parallelism between those disturbances and the epileptic attacks. The frequent occurrence of the attacks during sleep, that is, during a periodic process, as well as the intermittent character of the epilepsy may be connected with the sympathetic centers in the diencephalon. In the cases reported by the author, the epileptic attacks occurred during the hemiplegic as well as during the diplegic syndrome, in which pyramidal, extrapyramidal and mixed disturbances predominated. Among the patients with Little's disease who had epileptic attacks there were many who also had psychic disturbances. However, the incidence of the psychic disturbances was not higher than in other patients with Little's disease. In many of the cases of Little's disease with epileptic attacks, no anatomic basis could be found for the attacks. It is difficult

to make a definite prognosis regarding the reappearance of the attacks, even after prolonged observation. The treatment of the epileptic attacks in Little's disease should be like that of cryptogenic or of jacksonian epilepsy.

Rivista di Clinica Pediatrica, Florence

36: 961-1056 (Nov.) 1938

Nitrogen Metabolism and Utilization of Food by Infants Artificially Fed by Diet Constituted by Vegetal Proteins. A. Bieber.—p. 961.
*Influence of Lecithin and Lutein on Hypoglycemic Action of Insulin in Diabetes Mellitus. G. Pavan and C. Moro.—p. 994.

Lecithin and Lutein in Diabetes.—Pavan and Moro studied the influence of lecithin and lutein on the hypoglycemic action of insulin. In sixteen normal children and six normal rabbits the authors induced hyperglycemia by means of the administration of sugar and followed the behavior of hyperglycemia in the course of a test which consisted in the administration of an intramuscular injection of insulin alone, a lecithin and lutein preparation alone, lutein alone or insulin in association with any of the substances mentioned. In four children who were suffering from diabetes (mellitus or renal) the behavior of glycemia was followed after administration of either insulin alone, the lecithin and lutein preparation alone or insulin in association with this preparation. The authors found that the lecithin lutein preparation has a hypoglycemic action in normal children and in normal rabbits. Lutein has a slight hyperglycemic action, which is due to the fact that the substance on the market contains cholesterol. The lecithin lutein preparation when it is administered to children who are suffering from diabetes either after insulin or in association with it increases the therapeutic action of insulin, makes easy, slow and continuous assimilation of the drug by the patients, acts on the glycemia for several hours and thus prevents hypoglycemia. When insulin in association with the lecithin and lutein preparation is administered for about a month to patients suffering from diabetes, the figures of glycemia during fasting diminish. The dose of insulin can be reduced by this time. According to the authors, lecithin and lutein in diabetic patients stimulate transformation of dextrose into glycogen and also the capacity of the liver and muscles for storing glycogen.

Annaes Brasileiros de Gynecologia, Rio de Janeiro

4: 311-416 (Oct.) 1938

Hypophysis and Genitalia. C. Salgado.—p. 311.
*Estrogenic Substance in Treatment of Vulvovaginitis in Little Girls. L. Hoeppner Dutra.—p. 326.

Vulvovaginitis in Little Girls.—Hoeppner Dutra reports satisfactory results from the administration of estrogenic substance (progynon B) in the treatment of vulvovaginitis in twelve girls ranging in age from 2 to 10 years. The condition was gonorrheal in ten cases. The substance is given in intramuscular injections, once a week, at a dose of 10,000 international B units (U. B. I.) up to a total number which varies from one to three (and in rare cases four) injections. A vaginal lavage of a 1 per thousand protein silver solution is administered with a short fine sound every other day during the treatment. The mothers of the patients are instructed to put the patients in a sitz bath of tepid water for a few minutes every night. Generally the discharge stops and the gonococcus disappears from the secretion after the third injection. The evolution of the condition is controlled by making weekly examinations of smears prepared from the vaginal discharge. As the treatment advances the number of leukocytes and pus cells diminish in the secretion, the cells of the vaginal epithelium become vacuolar and cornified and the flora of the secretion becomes normal. In two of the cases seen by the author there was a complication of gonorrheal conjunctivitis which was rapidly controlled by the proper local treatment under the influence of the estrogenic treatment. The latter has an average duration of three or four weeks. It is not followed by complications. Recovery of the patients is permanent. According to the author the estrogenic treatment has a biologic action by which a cellular proliferation of the vaginal epithelium is stimulated, the reaction of the vaginal discharge is favorably modified (acidity) and the vaginal mucosa is regenerated.

Archiv für Gynäkologie, Berlin

167: 397-654 (Oct. 10) 1938. Partial Index

*Respiration and Capacity of Blood to Bind Oxygen During Pregnancy. W. Borgard and G. Effkemann.—p. 397.
Determination of Estrogenic Hormone in Blood and Urine During Delivery (Significance of Follicular Hormone to Delivery). G. Tsutsulopulos.—p. 403.
*Latent Period of Incipient Cervical Carcinoma and Duration of Freedom from Symptoms. E. Scipiades Jr. and K. S. Stevenson.—p. 416.
Behavior of Genital Apparatus of Female Rats During Prolonged Administration of Estrogen. Käthe Biedermann.—p. 465.
Hormonal Etiology of General Fetal Dropsy. E. Tscherne.—p. 489.
Modification of Vaginal Epithelium in Child by Means of Estrogen: Dosage of Estrogen in Gonorrheal Vaginitis in Children. K. Herrnberger.—p. 506.

Respiration and Blood Oxygen During Pregnancy.—During pregnancy, according to Borgard and Effkemann, respiration is altered in two respects: 1. As a result of the elevation of the diaphragm, the deep inspiration is mechanically impaired, the volume of the individual respiration is reduced and as a compensation the respiratory frequency is increased. 2. The total extent of the ventilation, the respiratory minute volume is greater than corresponds to the increased oxygen requirements of pregnancy (increase of basal metabolism during pregnancy). It has been pointed out repeatedly that the respiratory minute volume is increased by from 10 to 20 per cent during pregnancy. The authors subjected pregnant women to work tests in order to determine whether work requires a percental increase in the respiration compared to normal conditions and to what extent a changed oxygen combining power of the blood influences the respiratory minute volume. In a table the authors show the results which they obtained in twenty-seven tests. A comparison with the normal values of nonpregnant healthy women revealed that, with the same exertion, the respiration of pregnant women is considerably greater, although the absorption of oxygen per time unit is reduced as a sign of the decreased circulatory capacity during pregnancy. These quantitative determinations seemed necessary as a foundation for the investigation as to why the ventilation is increased during pregnancy. It was found that the increase in ventilation is due to an impairment of the conditions of arterialization in the blood. The curve recording the oxygen combining power of the blood of pregnant women is displaced toward the right even during rest; that is, a higher oxygen tension in the alveolar space is required than is the case in the absence of pregnancy. During exertion, the curve of the oxygen binding power of pregnant blood is essentially more toward the right than that of nonpregnant women.

Latent Period of Incipient Cervical Carcinoma.—In this extensive report, Scipiades and Stevenson review the literature on the problem of the beginning cervical carcinoma and report their own extensive studies. Summarizing their observations, they say that on the basis of cases that were selected from a clinical material over a period of twenty years it can be stated that the incipient cancer passes through a period in which there are no symptoms and the growth is not progressive. This latent period lasts at least six months and it may last six or even eight years, the average being about 3.9 years. The authors observed further that the carcinomas, which were detected early by means of exploratory excisions and which were treated by extirpation of the cervix, by radium irradiation or a combination of the two methods were always cured. Finally the authors demonstrated that the hyperactive epithelial changes can be regarded neither as precancerous conditions nor as incipient cancers, because they never developed into cancers. They gained the impression that these epithelial changes, just like the leukoplakias of the cervix, are fluctuating manifestations which, under the influence of different factors, may develop and disappear again. They say that it has been asserted that the surgical as well as the radiation therapy of the completely developed carcinoma has reached the limits of its possibility. They show that, if this is so, the only hope for further improvement is the earlier recognition of the carcinoma and they believe that the test developed by Schiller (staining with compound solution of iodine) and the colposcope devised by Hinselmann are valuable aids in facilitating an early diagnosis.

Klinische Wochenschrift, Berlin

17: 1457-1496 (Oct. 15) 1938. Partial Index

Action on Renal Function of Substances that Increase Blood Pressure. D. Schneider and P. W. Springorum.—p. 1460.
Antithyrotropic Protective Power of Blood of Healthy Persons and Patients. H. Eitel.—p. 1465.
Splenomegaly Verified as Boeck's Disease by Means of Sternal Puncture: Case. M. Dressler.—p. 1467.
Mode of Action of Prostigmine in Myasthenia Gravis. A. Lanari.—p. 1471.
*Nature and Diagnostic Significance of Triboulet's Reaction. H. Wiesbrock.—p. 1473.
Significance of Culture of Bone Marrow for Demonstration of Bacilli of Typhoid and of Paratyphoid. A. Ott.—p. 1475.
Differentiation of Whooping Cough Bacilli and Influenza Bacilli. A. Steigler.—p. 1480.

Triboulet's Reaction.—Wiesbrock points out that Triboulet's reaction is used chiefly for the diagnosis of intestinal tuberculosis but that, although it produces positive reactions in all cases of intestinal tuberculosis, it results in such reactions also in a large number of disorders and therefore cannot be regarded as specific for intestinal tuberculosis. In studies on seventy-four patients in whom intestinal tuberculosis was suspected, the author gained the impression that the protein bodies are demonstrable in the intestine in especially severe infections and intoxications. In order to throw more light on this problem, he made Triboulet's test on all specimens of feces, 550 in all, which were submitted to him for bacteriologic examination in order to detect typhoid, parathyroid or dysentery. In this material seventeen cases of typhoid were detected and the positive bacteriologic test was accompanied by a positive Triboulet reaction. In thirty-five cases of paratyphoid, in ten cases in which bacilli of the Breslau type were found, in sixteen of dysentery, in fourteen bacillus carriers and in a number of cases negative to bacteriologic examination Triboulet's reaction was found to be positive. It was also noted (although not always) that Triboulet's reaction produced a somewhat different type of precipitation in dysentery than it did in paratyphoid. Whereas the latter usually yielded a coarse precipitate and a clear supernatant fluid, the precipitate of dysentery often showed a fine granulation and a more or less clear supernatant fluid. Thus it was frequently possible to foretell the outcome of the bacteriologic test from the results of Triboulet's reaction. The author thinks that, if his observations should be corroborated by others, Triboulet's reaction could be employed as a diagnostic aid in infectious diseases of the intestine. The bacteriologic examination is often difficult, because bacilli are not always excreted with every stool. The author thinks that in large material it might perhaps be advisable first to subject the stools to Triboulet's test and then to make bacteriologic tests only on specimens in which Triboulet's reaction proves positive.

Münchener medizinische Wochenschrift, Munich

85: 1617-1656 (Oct. 21) 1938. Partial Index

Cardiovascular Xanthomatosis as Cause of Death in Young Persons: Contribution to Forms of Lipoidoses. H. Siegmund.—p. 1617.
*Pregnancy Polyneuritis and Its Relation to Vitamin B_1. A. Hildebrandt and H. Otto.—p. 1619.
Treatment of Lambliasis with Atabrine. K. Heilmann.—p. 1626.
Prevention of Infection After Accidental Injuries. C. Fervers.—p. 1628.
Occupational Arsenic Intoxications in Wine Growers. W. Frohn.—p. 1630.
Bullous Pulmonary Emphysema After Relapsing Infarct Pneumonia as Result of Accident. K. Bühler.—p. 1636.
Coxa Vara, Its Clinical Aspects and Treatment. M. Lange.—p. 1637.

Pregnancy Polyneuritis and Vitamin B_1.—Hildebrandt and Otto direct attention to the fact that treatment with vitamin B_1 is of great value in the polyneuritis of pregnancy. They report the clinical history of a woman who developed a severe polyneuritis during pregnancy. They instituted treatment with vitamin B_1 and vitamin C. The woman received during her pregnancy a total of 1,782 mg. of vitamin B_1 and there were no disturbing secondary effects such as premature elicitation of labor pains or symptoms of excessive dosage. The pregnancy terminated in the birth of a healthy child. Tests on the urine of the woman disclosed that up to the delivery no vitamin B_1 was eliminated in the urine and vitamin C was excreted in small quantities. Later, however, normal secretion was observed and vitamin B_1 could be detected in the serum. Not only did the administration of vitamin B_1 improve the pregnancy polyneuritis but the subacidity of the gastric juice and the hypochromic anemia were counteracted; the fasting blood sugar was slightly influenced (temporary slight decrease) and a hepatic disturbance was compensated. The authors conclude that, in the presence of severe paralytic symptoms during pregnancy, treatment with vitamin B_1 should always be tried before an interruption of the pregnancy is decided on.

Zeitschrift für Urologie, Leipzig

32: 649-720 (No. 10) 1938. Partial Index

Peridural Anesthesia. C. E. Alken.—p. 649.
*Phosphate Concrements of Urinary Tract. A. T. Jensen and J. E. Thygesen.—p. 659.
Therapy of Chronic Urinary Retention of Bladder (Hypertrophy of Prostate) with Transurethral Resection of Prostate. I. Farkas.—p. 667.
Combined Vesicovaginal and Ureterovaginal Fistula. E. Michadovski.—p. 680.
Roentgenokymographic Investigations on Normal and Abnormal Motility of Excretory Urinary Passages. M. Maintz, J. Meese and G. Wüllenweber.—p. 682.
Hypernephroma of Right Half of Horseshoe Kidney. G. Nicolich.—p. 696.
Pyocaneus Osteomyelitis of Vertebral Column Following Pyelonephritis: Case. T. Kusunoki.—p. 699.

Phosphate Concrements of Urinary Tract.—Jensen and Thygesen discuss recent developments in the chemistry of calcium phosphates and describe their studies on thirty-five phosphate calculi that had been obtained in renal and vesical operations and in the course of necropsies. In the qualitative analysis, sections of the calculi were pulverized and 0.25 Gm. of this powder was examined for carbonate, ammonia, phosphate, oxalate calcium and magnesium and in some cases also for uric acid and albumin. The analyses were always made in the same manner and the reactions were compared among one another and with the reactions of known quantities of pure substances. This method permits a rough estimate of how much of the various substances is contained in the calculi. The authors give an example of such an analysis. Further, roentgenologic diagrams were made of the pulverized calculi. These diagrams were then compared with the results of the analyses. In a few instances, diagrams were made also of the residue on ignition. The authors detected the following substances in the calculi: (1) magnesium ammonium phosphate, (2) a colloid-like calcium phosphate with incomplete apatite structure, which contains between three and three and one-half equivalents of calcium per mol of phosphoric acid and some closely bound water, and (3) beta-tricalcium phosphate. Those mentioned under points 1 and 2 are the usual constituents of phosphate calculi and they are found more frequently mixed than pure. Two calculi consisted of beta-tricalcium phosphate. So far it has not been possible to extract beta-tricalcium phosphate from aqueous solution but only by direct reaction between calcium oxide (CaO) and phosphorus pentoxide (P_2O_5) under high temperature. Calcium carbonate, normal magnesium phosphate and the secondary calcium phosphates, which are often designated as the usual constituents of phosphate calculi, were not detected.

Maandschrift voor Kindergeneeskunde, Leyden

7: 461-501 (Sept.) 1938

*Bacillary Dysentery in Young Nurslings. B. Lammerts van Bueren and J. H. de Haas.—p. 461.
Cases of Suprarenal Virilism. J. H. Smidt van Gelder.—p. 472.
Icterus Gravis: Case. J. H. Smidt van Gelder.—p. 478.
Klippel-Feil Syndrome: Case. A. van Westrienen.—p. 486.
Meningeal Manifestations in Presence of Ascarides. C. J. Wijckerheld Bisdom.—p. 490.

Bacillary Dysentery in Young Nurslings.—Lammerts van Bueren and de Haas report that among 400 children with bacillary dysentery observed at the children's clinic in Batavia there were 160 nurslings and eleven of these were less than 3 months old. On the basis of the clinical observations on these eleven young nurslings and of the bacteriologic examination of their feces, the authors conclude that bacillary dysentery may attack nurslings during the first three months of life, irrespective of whether they are bottle fed or breast fed. The course of the bacillary dysentery in these young nurslings is changeable and may even be fatal, just as in older children. Regarding

the etiology, the authors say that in the nurslings of the first quarter of life the same bacilli, the so-called pseudodysenteric bacilli, are encountered that are found also in the older children with bacillary dysentery. The dysenteric character of the feces is usually less pronounced in the young nursling than in older children. The diagnosis of bacillary dysentery requires the microscopic examination of the feces in the young nurslings as in the older children. It reveals a greater or lesser number of leukocytes and a few or no erythrocytes. The treatment of bacillary dysentery should be dietetic even in the young nurslings. Little or no medicaments should be given.

Acta Pædiatrica, Stockholm

23: 1-140 (Oct. 15) 1938

Comparison of Organic Acids and Sulfanilamide as Urinary Antiseptics. H. F. Helmholz.—p. 1.
White Blood Picture During First Year of Life, Especially with Regard to Its Course. J. H. Magnusson.—p. 14.
*Investigations of C Vitamin Standard in Healthy Children and in Children Suffering from Gingivitis. C. W. Herlitz.—p. 43.
Neuroblastoma in Left Adrenal with Intrathoracic Metastases. J. Reurink.—p. 78.
Experimental Studies on Conditioned Salivary Reflexes in Children. C. G. Bernhard.—p. 118.
Undesirable Tuberculin Reactions. H. Behrendt.—p. 129.

Investigations of Vitamin C.—Herlitz used the modified Lund and Lieck method of determining the content of ascorbic acid in the blood serum in forty-four healthy children without gingivitis and fifty-seven children with severe gingivitis, between the ages of 3 and 16 years, after the oral administration of 10 mg. of ascorbic acid per kilogram of body weight. It was found that the ascorbic acid content of the serum increased in the same degree to which raw fruit was added to the diet. This signifies an indirect control of the reliability of the food anamneses. The average fasting value for children who were given a moderate supply each day of raw fruit (approximately one orange or apple) in addition to an otherwise normal diet was 0.71 ± 0.073 and the two hour value, after loading, was 1.87 ± 0.111 mg. per hundred cubic centimeters of serum. The corresponding figures for children who, under otherwise similar conditions, seldom or at most received raw fruit only once a week were 0.24 ± 0.025 and 0.69 ± 0.05 mg. respectively. When the fasting values lie below 0.4 and, simultaneously, the two hour value is below 1 mg. the child has probably been receiving food poor in vitamin C content or a subnormal vitamin C standard is present. The existence of this combination of values does not in itself permit the diagnosis of scurvy. The probability that gingivitis has any connection with subnormal ascorbic acid was not elicited but that this condition must be referred to some other etiologic factors is suggested. Extremely low serum-ascorbic acid values may be made to rise to a normal level in three weeks by adding fruit to the diet in moderate amounts.

Ugeskrift for Læger, Copenhagen

100: 1069-1090 (Sept. 22) 1938

*Simple Urethritis or "Catarrh of Urethra": Comparative Experiences and Considerations on This Disease and Gonorrheal Urethritis. V. Genner.—p. 1069.
*Treatment of Infections of Urinary Tract with Calcium Mandelate: One Year's Experiences. E. Schnohr and C. Johansen.—p. 1074.
Infections of Urinary Tract Treated with Granulate of Calcium Mandelate. K. Rasmussen.—p. 1082.

Simple Urethritis and Gonorrheal Urethritis.—Genner says that, while simple urethritis in women is hardly as rare as commonly thought, his comparative statistics on this disorder and gonorrheal urethritis in more than 100 cases in men show a frequency ratio of 1 to 2. He asserts that the form of simple urethritis designated as "postgonorrheal catarrh" now constitutes only a small percentage of the total number of cases; its probable greater frequency formerly is ascribed to the more irritative treatment of gonorrhea then used. In about one third of the cases of simple urethritis there was history of earlier gonorrhea, but as a rule far back and without direct connection with the simple urethritis. Sulfanilamide seems to him an important addition to treatment.

Urinary Tract Infections Treated with Calcium Mandelate.—Schnohr and Johansen used calcium mandelate in the treatment of sixty patients with infections of the urinary tract. The dose was 12 Gm. daily and the amount of fluid ingested was limited to 1 liter daily. In thirty-nine cases the urine became sterile, in thirty-one after a week or less, in five after from nine to thirteen days, in three after twenty, twenty-five and sixty-five days respectively. In thirteen cases the subjective symptoms disappeared although the urine did not become sterile. The treatment was without effect in eight cases (six with complicating disorders, one with a history of ureterotomy, one in a pregnant woman given only two days' treatment). The urine became sterile in seven of twenty patients in whom the infection was a complication in a grave disorder of the urinary tract and in eight of thirteen cases with milder complications. The bacillary infection was eliminated in thirty-four of forty-seven cases with B. coli infection, in two of nine cases with B. proteus infection and in some cases with infection with staphylococci, gram-positive cocci and hemolytic streptococci. In most cases the p_H in the urine was reduced to between 4.8 and 5.3. As a rule the urine did not become sterile until the p_H was 5.3 or less, it was never sterile when the p_H was over 5.5. In six cases in which the p_H remained between 6 and 8 the addition of from 3 to 6 Gm. of ammonium chloride daily brought the p_H to about 5 in four and the urine became sterile in two. Except for a transitory hematuria in one instance, treatment with calcium mandelate caused no injurious effect on the kidneys although the renal function was impaired in several cases. Only two patients were unable to take the granulate because of gastric symptoms. Occasionally nausea occurred after some days' treatment, and in two cases there was nausea during the first days.

100: 1091-1126 (Sept. 29) 1938

*Osteomalacia of Spinal Column in Denmark in Cases with Deficient Diet or Diseases of Alimentary Tract. E. Meulengracht.—p. 1091.
Condition of Teeth at Bornholm. H. C. Olsen.—p. 1116.
Contact Ulcer. G. Hagerup.—p. 1117.

Osteomalacia of Spinal Column.—Meulengracht reports eighteen cases of osteomalacia in which the changes were localized chiefly in the spinal column. The subjective symptoms were pain in the back and groins, occasionally in acute attacks (spontaneous fractures). External examination established a settling of the back sometimes with kyphosis or lordosis. Often there was considerable decrease in height. Roentgen examination showed calcium deficiency in the skeleton, most marked in the spinal column; the vertebrae were low, biconcave or more irregularly deformed. Sometimes there was also a roentgenologically demonstrable osteo-arthrosis of the spinous process (Baastrup's disease) in the lumbar region, originated through the settling and shortening of the lumbar column. The changes are in some of the cases attributed to diet deficient in calcium and vitamin D; in the other cases gastric achylia or misuse of laxatives is believed through changed conditions of resorption to have been the contributing cause or the main cause for the development of the symptoms. Treatment with calcium salts and vitamin D proved effective.

Upsala Läkareförenings Förhandlingar, Uppsala

43: 267-464 (June 30) 1938

*Effect of Dextrose on Tar Tumors in Mice. K. A. Vannfält.—p. 267.
Roentgen Symptoms in Abdominal Injuries through Blunt Force. H. Laurell.—p. 413.

Effect of Dextrose on Tar Tumors in Mice.—Vannfält studied the effect of feeding 50 per cent dextrose solution on the growth and metastasis of tar tumors in mice and the length of life of the animals. In the females given dextrose there was a statistically established checking of metastases to the regional lymph nodes and to the lungs. In the mice with cancerous skin tumors the control group showed a statistically greater frequency of metastases (without regard to their localization) than the mice fed dextrose. The resistance of the animals with malignant tumors which expresses itself in greater length of life is considered a biologic indicator of the degree of malignancy. Since the animals given dextrose lived longer, the author thinks it probable that the tumors were less malignant than in the control group. Investigations on the effect of insulin on tar cancers in mice indicated that in the daily dose of 0.02 clinical unit it exerted no certain influence on the time of appearance of the tumor, its malignant degeneration or metastasis to the regional lymph nodes or internal organs but shortened the lifetime of the animals.